MAY, 1951

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

The Increased Incidence of Coronary Thrombosis in Chronic Peptic Ulcer

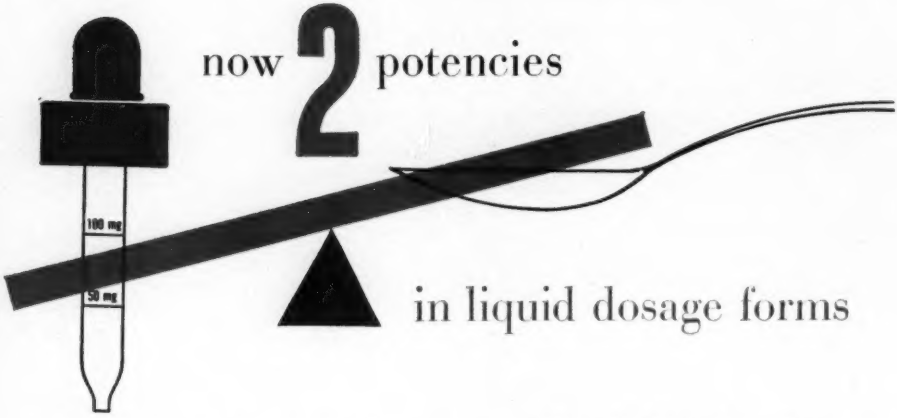
Gastroscopic Biopsy—Correlation of Clinical Findings and Tissue Biopsies of the Stomach

Clinical X-Ray Conference on Localized Constricting Lesions of the Colon

●

Sixteenth Annual Convention
Chicago, Ill., 17, 18, 19 September 1951

VOLUME 18 NUMBER 5



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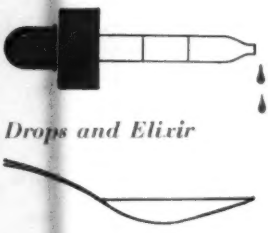

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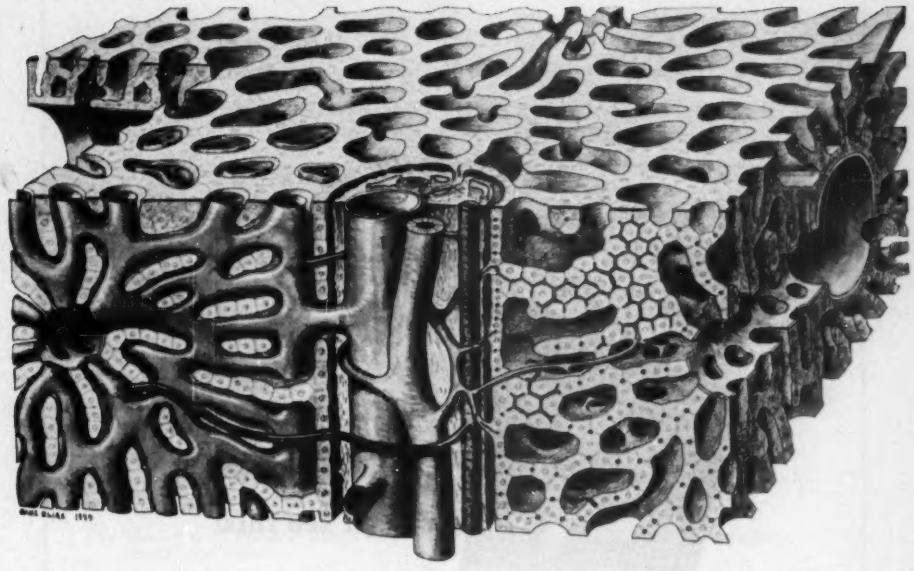

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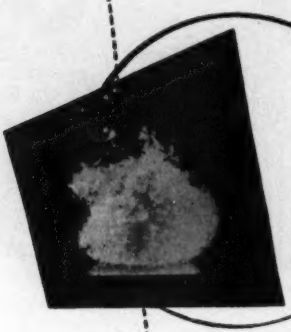

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The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

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The Review of Gastroenterology

OFFICIAL PUBLICATION

of the

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

1819 Broadway, New York 23, N. Y.

Editorial Office, 146 Central Park West, New York 23, N. Y.

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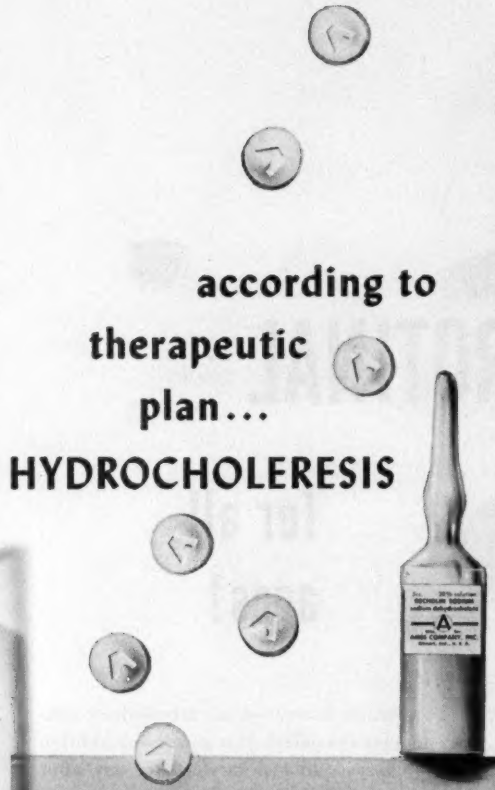

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A monthly journal of Gastroenterology, Proctology and Allied Subjects

Volume 18 MAY, 1951 Number 5

THE INCREASED INCIDENCE OF CORONARY THROMBOSIS IN CHRONIC PEPTIC ULCER*†

LESTER M. MORRISON, M.D.

Los Angeles, Calif.

The relationship of the stomach and the heart has been recognized and recorded by clinicians from earliest medical history. So close has this relationship been that only in recent times has the disease entity known as "death from acute indigestion" been recognized as acute coronary thrombosis.

The author demonstrated the effects of acute gastrointestinal disorders upon the coronary arteries 12 years ago at a previous annual meeting of the National Gastroenterological Association[6]. This was shown by simultaneous kymographic and electrocardiographic recordings from both the stomach and the heart in human subjects under clinical and experimental conditions. Today, however, I appreciate the invitation tendered me to bring to the attention of the Association the changes in the coronary arteries which result from chronic gastric disorders such as occur in chronic peptic ulcer.

From investigations carried out by Banting[1], Dock[2], Hall[3], Morrison[4], and others, there are 2 media whereby disease of the stomach can damage the coronary arteries. 1) The late Sir Frederick Banting[1] and his co-workers demonstrated that prolonged and intense vagal stimulation in the dog and other experimental animals resulted in a) the creation of peptic ulcer and b) the simultaneous development of coronary thrombosis. In the same way Soma Weiss demonstrated the vago-vagal syndrome—or the acute effects of vagal stimulation upon the coronary arteries; this mechanism was shown in detail by Morrison and Swalm[4,6] from experimental gastric and esophageal distention which caused angina pectoris in atherosclerotic patients. At the same time the author revealed the electrocardiograph changes such as inversion of the T waves, depression Q-R-S complexes,

*Read before the Fifteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 9, 10, 11 October 1950.

†From the Department of Internal Medicine, College of Medical Evangelists.

Aided in part by grants-in-aid from the Los Angeles County General Hospital and the American Medical Association—Committee on Therapeutic Research, Council on Pharmacy and Chemistry.

Grateful appreciation is expressed to my co-workers, William F. Gonzalez, M.D., Perla Berlin, B.S. and H. Bergman, Ph.D. for their aid in these studies.

etc., which accompanied the angina from the gastrointestinal distention. These findings in human and experimental subjects were subsequently confirmed by Gilbert and Fenn[7] and others.

2) Recent impetus to the dietary concept of atherosclerosis has been given by the work of many investigators such as Dock[2], Hueper[8], Moreton[9], Snapper[10], Gofman[11], Plotz[12], Morrison[13] and others. These authors have shown that the excessive ingestion of dietary fat and cholesterol increases the incidence of coronary atherosclerosis. Alimentary hyperlipemia has been studied with the resultant great increase in blood plasma chylomicron and lipomicron counts as well as increases in total blood serum lipids and neutral fat fatty acids. Serum cholesterol and cholesterol esters can be made to rise only after prolonged ingestion of excessive dietary fat and cholesterol intake. Such diets must be persisted in for periods ordinarily averaging one or more years before significant rises in serum cholesterol and esters will occur.

The gastroenterologist or clinician is immediately faced with the problem of the dangers involved in the Sippy dietary regime for peptic ulcer. If the prolonged ingestion of dietary fat and cholesterol is persisted in experimental animals such as the rabbit, the chick and the dog with modified thyroid function, atherosclerosis develops in the aorta and coronary arteries as shown by Anitschkow[14], Steiner[15], Broun[16], Morrison[17] and others. Do the same effects occur in patients with chronic peptic ulcer who are on prolonged Sippy diets with frequent milk and cream feedings and emphasis on fat ingestion to inhibit gastric acid secretion, gastric peristalsis, motility with pyloro- and duodenal spasm? No direct proof has been offered to confirm or deny this question. Only indirect evidence has been presented to date and clinicians have therefore been obliged to continue the Sippy dietary regime in the treatment of peptic ulcer in the absence of convincing evidence to the contrary.

It is surprising to discover from the literature that only one attempt has been made to learn whether an increase in coronary atherosclerosis occurs in chronic peptic ulcer. This attempt was made by Walsh et al[16] who studied the records of autopsy material. It was found that only a gross estimate or grading of the coronary arteries was possible, as it had been estimated in routine autopsy material. The essayist tried this approach and in a recent report[17] found that such a method was subject to so many variables that the information gained by a gross evaluation of coronary atherosclerosis was undesirable. In the foreign literature several authors have mentioned an increase in coronary symptoms among peptic ulcer patients[26-28].

My co-workers and I examined the autopsy records in a large series of consecutive chronic peptic ulcer patients at the Los Angeles County General Hospital. Instead of asking for the comments of the pathologist or resident as to the gross appearance of the coronary arteries, we selected cases only with proven coronary thrombosis and myocardial infarction. As has been shown by the author and others, this is the only conclusive demonstration of coronary atherosclerosis, since

thrombosis with infarction occurs in over 90 per cent of cases of coronary atherosclerosis.

The accompanying Table I shows the results of our survey of over 1,000 consecutive cases of both sexes studied for evidence of coronary thrombosis and myocardial infarction. From this material we studied 116 consecutive cases who died of chronic peptic ulcer (both sexes) and found that 27 showed evidence of one or more instances of coronary thrombosis and infarction which had occurred at some time in the past prior to death caused by a complication of chronic peptic ulcer. This placed the incidence of coronary thrombosis in peptic ulcer as 23 per cent. No accurate distinction could be made in these cases between patients who had adhered to a Sippy diet and those who had not. Our controls consisted of 71 consecutive cases who had died of an acute illness other than that caused by cardiac disease or peptic ulcer. We found that 6 or 8 per cent of these cases were found to have had a previous coronary thrombosis with myocardial infarction. As a further control we studied 152 consecutive cases who had died of chronic

TABLE I

INCIDENCE OF CORONARY THROMBOSIS WITH MYOCARDIAL INFARCTION AT AUTOPSY

Cause of Death	No. of Cases	No. & % with Coronary Thrombosis	Mean Age
Acute Diseases	71	6 (8%)	51
Chronic Diseases	152	17 (11%)	50
Chronic Peptic Ulcer	116	27 (23%)	58

diseases other than cardiac ones or peptic ulcer. In this series we found 17 or 11 per cent of patients who had experienced a coronary thrombosis with myocardial infarction in their past.

For further comparison (Table II) we studied 100 consecutive cases who died of diabetes mellitus and found that 24 or 24 per cent had had a previous coronary thrombosis with myocardial infarction. Two hundred consecutive cases who died of "alcoholic" cirrhosis of the liver had 10 or 5 per cent of cases with coronary thrombosis and myocardial infarction. Seventy consecutive cases who died of thyrotoxicosis revealed an incidence of 4 per cent with coronary thrombosis and myocardial infarction. One hundred consecutive cases who had died of malignant neoplasms revealed an incidence of 6 per cent of coronary thrombosis with myocardial infarction. A detailed breakdown of this data was presented in a recent report[25] by the author.

Statistical analysis by the chi-square test of the summarized data in Table I indicated that the incidence of myocardial infarctions among patients with chronic peptic ulcer was significantly greater than among those with other diseases (both acute and chronic). The p values were far less than 0.001 in all the comparisons.

Inspection of the data distributed as to sex and age decades showed that the incidence of myocardial infarction varied in much the same pattern for all the groups.

This investigation showed clearly that coronary atherosclerosis was considerably greater in chronic peptic ulcer than in controls, as evidenced by the statistically significant increase in coronary thrombosis with myocardial infarction.

The exact mechanism of this increase cannot be exactly defined at this time. This mechanism may operate through one or both of those described in the preamble of this presentation.

Chronic or continual stimulation of the gastric vagus nerve alone may mediate these changes in the coronary arteries. Prolonged, excessive ingestion of large quantities of milk, cream, butter and eggs such as required in the Sippy diet may also be responsible for coronary atherosclerosis leading to ultimate coronary thrombosis with myocardial infarction. A combination of both these etiologic vagal

TABLE II

POSTMORTEM INCIDENCE OF CORONARY THROMBOSIS WITH MYOCARDIAL INFARCTION IN PATIENTS WHO DIED OF VARIOUS DISEASES

Cause of Death	Tot. No. of Cases	No. with Cor. Throm.	% with Cor. Throm.
Acute Diseases	71	6	8
Chronic Diseases	152	17	11
Diabetes Mellitus	100	24	24
Thyrotoxicosis	70	3	4
Malignant Neoplasms	100	6	6
"Alcoholic" cirrhosis of the liver	200	10	5
Chronic Peptic Ulcer	116	27	23

and dietary agents in chronic peptic ulcer may act synergistically in the production of coronary atherosclerosis.

As the author has shown in previous reports[18], brief periods up to 3 months of daily excessive fat and cholesterol ingestion (milk, cream, butter and eggs) will not significantly elevate serum cholesterol and/or esters in the majority of patients. It is only when the chronic ulcer patient consumes large quantities of daily milk, cream and eggs over years that serum cholesterol and esters as well as the chylo- and lipomicron counts, together with total lipids and neutral fats often rise significantly. The converse is also true, i.e. that rigid restriction of dietary fat and cholesterol intake over several years will significantly reduce the total serum lipid fractions in most cases.

It should be here pointed out that hypercholesterolemia does not necessarily imply an increased tendency to the development of coronary atherosclerosis in all cases, although it does in a large proportion of individuals as pointed out by Steiner[22],

Adlersberg[19], Wilkinson[20], Dock[2], Morrison[21], and others. It is well known that many individuals with marked hypercholesterolemia have minimal atherosclerosis, due to the favorable phospholipid/cholesterol ratio, as shown by Kellner[23], Ahrens and Kunkel[24], and others. This ratio is normally well over one, indicating that the phospholipid stabilizes and disperses the serum cholesterol and esters in a stable colloidal state in the blood stream, retarding or inhibiting the development of atherosclerosis. The liver regulates this phospholipid turnover and function to a large extent. In addition it has been recently shown by Gofman and co-workers that pathological cholesterol-protein molecule complexes are the cause of coronary atherosclerosis. These giant pathological molecules of low molecular density are not necessarily related to a quantitative increase in serum cholesterol levels although they are more frequently found in hyperlipemia due to increased dietary fat and cholesterol intake.

In conclusion, although it can be definitely stated that an increase in coronary atherosclerosis occurs in chronic peptic ulcer, it is suggested that the mechanisms of this increased incidence may be in a) excessive, prolonged stimulation of the gastric vagal nerve supply with reflex effects on the coronary arteries; and b) possibly the excessive, prolonged daily dietary intake of fat and cholesterol, extending over a period of years. It cannot be as directly proven that this increase is related to increased dietary fat and cholesterol ingestion. Indirect evidence, however, indicates that a prolonged increase in daily dietary fat and cholesterol intake predisposes to the development of coronary atherosclerosis in susceptible individuals. An evaluation of the effects of prolonged Sippy diets and/or the use of dietary protein supplements instead of whole milk and cream feedings in peptic ulcer is merited.

Summary

1. There is a substantially increased incidence of coronary atherosclerosis, and of coronary thrombosis with myocardial infarction in chronic peptic ulcer.

2. An evaluation of the prolonged use (extending over years) of excessive, daily dietary fat and cholesterol intake in chronic peptic ulcer patients merits consideration as a potential cause of coronary atherosclerosis and coronary thrombosis.

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Discussion

Dr. David Adlersberg (New York, N. Y.):—Dr. Morrison was kind enough to send me his paper and I enjoyed studying it. I believe that he established well his conclusions, and I am glad to see that the data are statistically significant. The incidence of coronary thrombosis in 20 per cent of the patients with peptic ulcer, versus 7 or 8 per cent in the control group, is of (statistical) importance. Actually my plan as a discusser of this paper is to reemphasize a few points that he has discussed, and to add an explanation as to how the association of these two disorders could be explained.

This paper is important, first of all, because of the increased interest in degenerative diseases. Our thinking in medicine, as you know, has been always influenced by trends and fashions, and today medicine is interested in degenerative diseases, two representatives of which are arteriosclerosis and peptic ulcer. Secondly, there is increasing interest in the metabolic aspects of arteriosclerosis. You are probably all aware of the fact that until recently arteriosclerosis was considered to be a wear and tear phenomenon, an unavoidable consequence of the aging process of man. Only recently facts became evident suggesting that arteriosclerosis is not simply a manifestation of aging but a metabolic disease, which occurs more frequently in old persons than in young people.

In this connection, it must be stressed that 10-15 per cent of the aged population present evidence of senescence of the vessels, like dilatation and elongation, without signs of arteriosclerosis; on the other hand extensive arteriosclerosis with fatal termination may be found in young individuals. The interest in the metabolic and genetic aspects of arteriosclerosis led to important observations. A disturbance of lipid metabolism is considered to be a predisposing factor in the genesis of, at

least, certain forms of atherosclerosis. An elevation of serum cholesterol, an abnormal serum cholesterol/phospholipid ratio, an increased concentration of low density lipid and lipoprotein components of the serum (determined by the ultracentrifuge method of Gofman et al) and even the number and size of chylomicrons in the serum have been considered. The role of these factors in the genesis of atherosclerosis is still under investigation and not fully understood. It is also important that of these factors at least hypercholesteremia represents an inborn error of metabolism. The genetic transmission of this disturbance of lipid metabolism was studied by us and others.

This paper is also important because it touches upon the practical question of how to feed our patients with chronic peptic ulcer. You are probably familiar with the work of Dr. Plotz, of Brooklyn who warned against the use of the high fat, high cholesterol Sippy diet in patients with peptic ulcer and angina pectoris. Additional observations in this field are necessary.

I may mention briefly that some continental pathologists are of the opinion that the importance of lipids in the etiology of atherosclerosis has been overemphasized. Studies of the earliest lesions in the aorta and the coronary arteries led Roessle, Mayer, Sinapius and others to believe that the deposition of protein material in the intima is of paramount importance. On the other hand there is a certain tendency to emphasize inflammatory lesions of the arteries as the primary cause of some forms of atherosclerosis. Von Albertini has revived the old concept of Virchow (and some other German and French pathologists) according to which the primary cause of arteriosclerosis may be coronary arteritis. Superimposed secondary arteriosclerosis may completely mask the primary inflammatory disease of the arterial wall. It is extremely difficult to find coronary arteries or other small or large arteries in which these inflammatory lesions are still visible and not covered by plaques of secondary atheroma.

Dr. Zak and I had the opportunity to study fifty young individuals who died of coronary occlusion at Mount Sinai Hospital. The youngest individual of this group, a man of 27 years, had practically no arteriosclerosis of the coronary or peripheral arteries but presented a stenosing coronary arteritis with heavy infiltration of polynuclears in the intima and in the media with a superimposed occluding thrombosis. Stenosing coronary arteritis was more frequently encountered in another group of young individuals who died suddenly of coronary occlusion (material of the Chief Medical Examiner's Office).

In view of the revived interest in inflammatory coronary lesions as a basis for some forms of coronary atherosclerosis it is important to recall that there also exists a vascular theory of peptic ulcer (Von Eiselberg and others) in which vascular thrombosis plays an important rôle. Accordingly in a few papers of recent years the simultaneous occurrence of ulcer and coronary artery disease in the same person was explained as the manifestation of the same disease in two organs (Hochrein and Schleicher, 1941). Robert Junet of Geneva suggested that the peptic ulcer and the coronary artery disease are not two diseases *sui generis* but different localizations of the same pathogenic principle. Uehlinger, a well-known Swiss pathologist,

considers the possibility that peptic ulcer and coronary artery disease in the same person represent manifestations of inflammatory vascular disease.

I am fully aware of the fact that Dr. Morrison discussed carefully the other possibilities for the frequent occurrence of coronary artery disease and peptic ulcer. He stressed the well-established rôle of vagal stimulation and the vago-vagal mechanism. I presented another theory according to which a common vascular factor of arteritis could explain the association of these two disorders, at least in some patients of this group.

Dr. Maurice Feldman (Baltimore, Md.):—In a recent study on an appraisal of the psychological relationship of coronary disease to peptic ulcer, which will be published in the "American Journal of Digestive Diseases", we noted that among 753 autopsies there were varying degrees of arteriosclerosis of the coronary arteries. Among these we found 152 cases with coronary occlusion, an incidence of 20 per cent. Of the 753 cases, there were 68 with peptic ulcer, an incidence of 9 per cent. Of the 152 cases of coronary occlusion, peptic ulcer was present in 16, or an incidence of 10.5 per cent. Although the incidence of peptic ulcer seemed to be somewhat higher than in the general autopsied population, statistically this is not believed to be significant.

Others have studied this problem and have shown that there is no relationship whatsoever between the two conditions; however, in our studies we have noted that there are a number of similar factors common to both conditions: (1) Both occur in nervous, unstable individuals; (2) Both have three basic phenomena; namely hypersensitivity, hyperirritability, and hyperactivity; (3) Both occur predominantly in the nonphlegmatic individuals; (4) Both occur more commonly among the more intelligent and educated people and especially amongst executives; (5) Both have periods of intermittency and periodicity of symptoms; (6) A similarity of personality changes occurs in both conditions; (7) Both seem to have a latent period; (8) The aggravating effects in both are not too dissimilar; (9) Both occur more commonly in males and in the white race; and (10) Both groups live beyond their normal tempo and capacity.

Although both conditions apparently seem to fall into a similar psychosomatic pattern, there is probably no definite relationship between the two conditions.

The discrepancy between Dr. Morrison's and our statistics was obvious. His were compiled from a clinical series of peptic ulcer cases, whereas ours were compiled from a series of autopsy cases of coronary occlusion.

Dr. Hyman I. Goldstein (Camden, N. J.):—Adsorbents and antacids with milk, cream, eggs, butter, and other high cholesterol foods have, for many years, been used by thousands of ulcer patients. Since smoking and drinking (alcoholics) are not now limited to the men, but indulged by women (often too much) ulcer has become more common in women than formerly. The tobacco smoking habit—chain smoking—is frequently seen among women, too, and, so we meet, in this speedy fast-living era, with all of the daily excitement—increasing numbers of coronary cases among both men and women.

As you well know, Sir Gilbert Blane (1796) recommended antacids, alkaline earths, kaolin, carbonates, milk of magnesia, milk for high gastric acidity and, Paul Aegineta (625-690 A. D.), Verandæus, Scultetus, the great Spigelius, and other ancient writers used aluminum silicate (kaolin) or terra Sigilleta, and milk, and honey, and soft smooth diet—Celsus, too, recommended the "avoidance of all acid and acrid substances; and a smooth soft diet for ulcer".

It is important to know what to do for patients who have had a gastric or duodenal ulcer, and who develop coronary thrombosis, and are given anticoagulant therapy—tromexan, heparin, dicumarol. These patients, while under anticoagulant therapy, may develop gastroduodenal hemorrhages. Protamine and toluidine-blue must be administered intravenously, together with blood transfusion—and the anticoagulant must be stopped. These complications, fortunately, do not often occur—but it is a source of anxiety and worry, when it does occur! Now, in Samuel I, Chapter 25, verses 36-38, of the Old Testament—you recall the story of David and Nabal and his wife Abigail. David had threatened Nabal—because of his churlish and evil refusal to part with some of his holdings, and so, his wife (Nabal's) Abigail of good understanding and of a beautiful form, made haste and took 200 loaves of bread, wine, sheep ready dressed, parched corn, raisins, figs and laid them on asses, and with her young men servants (without telling her husband) rode on her ass to visit with David (who did like the ladies), and to appease him—which she did successfully. Upon her return she found Nabal "very drunken" and she waited for morning, when she confessed all that she had done to appease David, to save Nabal's life. Because of his anger and excitement at hearing all these things (psychosomatic medicine), his heart died within him and became as a stone. And it came to pass about ten days after this attack of coronary thrombosis, that the Lord smote Nabal, so that he died of his myocardial infarction and, probably, second coronary occlusion, and David took Abigail as (another) wife!

The Old Testament probably was compiled about 975 B.C.-1000 B.C., and also, during the Homeric era. Well, Homer, in his Odyssey, Book III, tells of the escape from enemies by Menelaus—through stormy seas and raging winds, but at Sunium, the sacred headland of Athens, Phoebus Apollo (God of Archery and the Sun) shed down his darts upon Menelaus' navigator and poor Phrontis, son of Onetor, the leading pilot and boatman of the tribe, dropped dead following the great excitement and exertion in skilfully holding the ship to her course through the thick and heavy squalls, the piercing winds and monster waves, with the steering oar of the moving ship yet grasped within his hands! Phrontis dropped dead from acute coronary occlusion and myocardial infarction. I do not have the electrocardiograms in this case!

Sophocles (497 B. C.-406 or 405 B. C.), the author of famous tragedies—Triptolemus (when 28 years old), Ajax, Antigone, Oedipus Tyrannus, Oedipus at Colonus, the Electra, and over a hundred others—had publicly competed, and recited his plays,—with Euripides and Aeschylus (525-456 B. C.), father of Greek drama, and was friendly with Herodotus and Pericles.

On this occasion Sophocles (at 91 years) was competing with Euripides, he excitedly, and with much effort, recited his Antigone, and when declared the winner,—from joy, excitement, and physical exertion dropped dead from acute coronary occlusion! Again, I have no electrocardiograms!

In "Oedipus Tyrannus" 961—Sophocles speaks of *"A little stroke puts aged bodies to sleep"*, and Walter C. Alvarez in recent years, has talked about "little strokes".

Archangelus Piccolomini (1526-1586) in his *"Anatomical Prælectiones"* (1586), said: "I am of the opinion that obliteration (or occlusion) of the little cord or vessel (or "nerve") which goes to the heart, suddenly brought on, is the cause for which some persons go suddenly and unexpectedly out of this world."

Finally, may I recall to you the reports by Seneca, who suffered from angina pectoris and coronary occlusion, in his 54th Letter to Lucille; Leon-Louis Rostan in his "Memoire sur les ruptures du Coeur" (1820); Frederick Winsor (1829-1889); Adam Hammer (1878); and the case reports by William Harvey, of the deaths of Nobleman Sir Robert D'Arcy, and the young Lord Montgomery from rupture of the left ventricle, following attacks of coronary occlusion and myocardial infarction!

Question:—I should like to ask one question, whether Dr. Morrison has found a relationship between this and a gallbladder cholesterosis and the cholesterol gallstone.

Dr. Frank R. Fabiani (Dobbs Ferry, N. Y.):—There is one point about diet which I think is to be stressed. I think Dr. Bruger, here in New York, made some very interesting observations so far as cholesterol relationship to arteriosclerosis are concerned. He pointed out that among the Chinese arteriosclerosis and atherosclerosis are practically unknown, yet when they come to our civilized diets of America, they develop diseases common to us. They live on a rice diet and do not develop the diseases that we do.

The relationship of smoking to arteriosclerosis is something which I think has been overrated. Dr. Bruger brought out the point that the Arabs, who will go into the desert for four or five days at a time without any food, and the only thing they partake of is smoking their pipes for hours at a time, do not develop any symptoms of atherosclerosis. In experimental animals and patients the relationship of iodides to cholesterol level in the blood is very important. If cholesterol is given in high animal fat diets, they will develop hypercholesterolemia, but if given in association with iodides, that does not take place. The iodides maintain a normal cholesterol level. It will not influence an already present hypercholesterolemia.

Dr. Horace W. Soper (St. Louis, Mo.):—I ask the question, when we take them off the rich cream and egg emulsion, and so on, what are we going to do? Baby foods, Gerber's and Libby's, homogenized vegetables and fruits, rice, as the doctor said, and foods of that character.

Now, you can feed all the white of egg you like, because in Bridges' Table of Cholesterol Foods, white of egg is the only one that contains absolutely no cholesterol, so you can feed all the white-of-egg desserts you like, if you leave out the

yolk. The yolk, according to Bridges, contains 3,500 mg. to the 100 c.c., while beef and mutton, and chicken, lean, contain only 60 or 80, so you can feed these patients ground beef, and ground meats, avoiding the fats. Never feed them any internal organ of any kind, not even fish eggs, which are very high.

Dr. Hyman I. Goldstein:—Egg albumen contains lysozyme, and if there is anything in the story of lysozyme in relation to ulcerous disease—

Dr. Soper:—No. White-of-egg desserts are all right. In our clinic we have followed this for many years. Every patient over the age of thirty-five is put on that diet instead of the usual diet that we use in younger persons with ulcer.

Dr. Lester M. Morrison (Los Angeles, Calif.):—I should like to thank Dr. Adlersberg very much for his discussion and comments, since he is one of the pioneer investigators in this field. I have learned of additional workers from his discussion today. Banting's death was a tremendous loss not only to the world in general, but to this problem itself, because immediately before his death he, Hall and Manning, had planned further studies following these original dog observations with vagal stimulation, demonstrating the frequency of the occurrence of both coronary thrombosis and peptic ulcer in experimental animals.

I was very much perplexed by the question that Dr. Adlersberg raised with regard to the common vascular factor. It certainly is one that has to be considered and one which I am at a total loss to explain or to understand. There has been so much speculation, and so many opinions given regarding this, yet there has not been adopted as yet an adequate experimental method of investigating this question in humans during the activity of these lesions. I think that on further study it may certainly shed a good deal of light on that question, and I want to thank him for raising it.

I enjoyed Dr. Goldstein's discussion hugely. As always, it is a delightful experience to hear him, and I always learn a great deal from his historical discussions. I wish to thank him for that.

I should like to attempt to answer the question that was raised with regard to the relationship between gallbladder disease, cholesterosis, and coronary atherosclerosis. As you all know, the original relationship between the pathological gallbladder and the coronary arteries was made at the University of Pennsylvania by members of the Cardiac Section in the Robinette Foundation. These workers demonstrated reversion of abnormal electrocardiographic T-waves and Q.R.S.-complex changes of pathologic character in patients with diseased gallbladders, which returned to normal following cholecystectomy.

Now, in the paper by Walsh and White, which I quoted, it was stated that there was no increase in the relationship between chronic gallbladder disease with gallstones, and coronary atherosclerosis, but this, again, was based on the gross inspection of the coronary arteries and again is quite open to question as to interpretation.

Those points were well taken in regard to iodides, which have also been shown by John Gofman in ultracentrifugal studies.

In response to Dr. Feldman's comments our cases were all deaths from peptic ulcer because in our statistical survey we found no appreciable difference from the controls in the incidence of ulcer in patients who died of coronary thrombosis. However, the incidence of thrombosis in the ulcer cases who died primarily of one of the complications of ulcer was twice as great.

I agree with Dr. Feldman heartily as to the psychosomatic relationships present in both ulcer and thrombosis. I think these are very well borne out by the recent studies of Flanders Dunbar, Franz Alexander and others with regard to the psychosomatic patterns that occur in ulcer groups and thrombosis groups. With Dr. Georgene Seward, psychologist at the University of Southern California, we have been studying gastrointestinal psychosomatic patterns for the past two years. We have also noticed that there is a great deal of overlapping between personality traits which are common to various disorders.

I too was struck by the figures published two months ago in "Circulation" by White and Dry, which showed that of the males in America up to the age of fifty, over half the individuals have at some point or other in the coronary arteries an atherosclerotic lesion projecting in up to 50 per cent of the lumen of the coronary artery.

Our figures, which were published one month later in "Geriatrics", were practically the same for males. We did not study the females, as they did. We estimated that by the time the average man reaches the age of fifty in this country, he has developed at one point or other in the left or right coronary arteries at least 50 per cent of closure of the lumen. I therefore think Dr. Feldman's point is very well taken in that regard.

Once again I should like to thank the Association for the invitation to present this work and to thank the discussers for their stimulating discussions.

THE EVOLUTION OF SURGICAL SUPERVISION IN THE MANAGEMENT OF ADVANCED IDIOPATHIC ULCERATIVE COLITIS*†

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and
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Chronic idiopathic ulcerative colitis, in all probability, has been a disease that has afflicted mankind for many centuries despite the none too prevalent or clear descriptions of the disorder in early medical literature. It has commonly been confused with the bacterial dysenteries and, even until recent years, was considered merely a chronic form of these infections. Cruveilhier (1829-42) illustrates the disease in a colored drawing. In 1875, Wilke and Maxon referred to its pathology in their lectures. A typically diseased colon was exhibited by Allchin, in 1885, at the Medical Society of London, and in 1888, W. Hale-White described the condition well[1].

During the latter part of the nineteenth century, surgical intervention as a form of treatment became recognized. Some form of enterostomy was the procedure of choice, but it is difficult to state just who performed the first ileostomy for ulcerative colitis. Enterostomies had been practiced prior to the nineteenth century for intestinal obstruction. In 1675, Paul Barbette, of Amsterdam, advised laparotomy in obstinate cases of volvulus and intussusception and a few years later, Nucke, the anatomist, successfully carried out this procedure[2]. Morgagni early in 1700 proposed operative intervention for cancer of the rectum, and in 1739, Faget first attempted it[3]. Renault, in 1772, performed the double operation of gastrostomy (abdominal section) and enterostomy[2]. In 1776, Pillore is credited with having performed the first colostomy for carcinoma, and in 1823, Reybard resected the sigmoid flexure for carcinoma. By 1880, only ten resections had been reported and only three of these were successful[3]. Colon surgery was delayed because of the frequent and always fatal complication, peritonitis. Block, of Copenhagen, in 1891, discovered that this could often be prevented by extraperitonealizing a segment of large bowel and with this advance, mortality was greatly reduced.

Follet of Lille, France, in 1885, introduced the surgical treatment of ulcerative colitis by employing a cecal fistula in order to divert the fecal stream from the diseased colon[4]. Howard Lilienthal[5], a proctologic surgeon, in 1899 was one of the first Americans to perform colectomy for an intractable case of ulcerative colitis. His patient, a young woman of 25 years, successfully survived the operation, and in a report by Cave[6], in 1939, the patient was noted as still being alive.

Surgical management for ulcerative colitis at the turn of the century assumed two fairly distinct courses. In one, enterostomy was undertaken as a palliative measure to divert the fecal stream and was accompanied by rather high mortality

*Read before the Fifteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 9, 10, 11 October 1950.
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rates. In the other form of treatment, enterostomy was utilized for the purpose of medicating the bowel. In 1902, Weir is credited with being the first to use the vermiform appendix as a passage for irrigating the colon[7]. In the next two decades, appendicostomy gained in popularity and even today we find many European as well as some American surgeons employing it as a direct approach to treating the diseased colon.

Wallis[8], writing in 1909, lists appendicostomy as the most important form of operative intervention. He classified cecostomy and colostomy as alternate measures but less efficacious. These procedures allowed for the flushing of the colon by a warm solution of soda bicarbonate. A small Kelly's tube was passed into the rectum to allow the fluid to freely escape.

During the 1920's, treatment by direct irrigation through appendicostomy or other openings lost in popularity and soon became superseded by methods directed to interrupt the passage of intestinal contents into the diseased colon. Ileostomy, uncommonly performed prior to 1910, became more prominent and though at first widely practiced, was later reserved as an emergency or life-saving measure only. According to Bargen et al[9], the number of patients in their series who underwent ileostomy during the time from 1913 to 1921 was greater than during subsequent periods. The reason for this was believed to be due to the inadequacy of medical management in those years. Mortality was high due to the performing of ileostomy too early in the course of the disease as well as its institution in fulminating cases.

Indeed, until recent years, specific measures for medical management were entirely lacking and in the severe forms surgical intervention was deemed the only effective therapeutic choice.

With the advent of more and more successful resections for cancer of the colon and rectum, segmental removals of parts of the diseased colon following the establishment of a permanent ileostomy were attempted and the results were surprisingly successful. With preparation of the bowel by sulfonamides, the surgical risk was reduced and more extensive resections became possible. Colectomy, at first, was always a multiple stage procedure, the first step being performed about six months to a year after an ileostomy had been established. Usually, the first stage consisted in the removal of only the right colon, but later the resection was extended to the mid-transverse large bowel. This allowed the remainder of the colon down to the sigmoid to be extirpated in a second stage. Sometimes three stages were carried out before the terminal large bowel was reached. The last stage consisted in the abdominoperineal excision of the rectum and remaining sigmoid colon. At the termination of each abdominal stage, the remaining sectioned end of colon was seldom closed and allowed to fall back into the abdominal cavity but was brought out to form a mucus fistula.

At present the stage method of colectomy has been simplified to include, usually, only three steps. In the first, an ileostomy is performed; in the second, the colon with a segment of terminal ileum is resected down to the sigmoid which is utilized

to form a sigmoid colostomy. In the last stage, an abdominoperineal excision is carried out with removal of all of the remaining bowel.

Further reduction in the number of stages has been forthcoming in the past few years. Miller[10,11] reports primary colectomy with ileostomy, and Lahey[12] cites a single case in which colectomy and removal of the rectum were performed in one stage. Primary colectomy with ileostomy has been practiced by us in selected cases[13].

Indications for Surgery

From 15 to 20 per cent of patients with idiopathic ulcerative colitis undergo surgery in the management of their disease. By far and large, the majority of these patients have advanced and irreversible alterations of the colonic mucosa, often with involvement of the other layers of the wall, and occasionally abscess and fistula formation are found. Tubular strictures are not uncommon. Pseudopolypoid formation is frequently present during exacerbations of the disease and in the fulminating forms. In long-standing cases, adenocarcinoma is by no means a rare catastrophe.

Most commonly, surgical intervention is invoked because of the intractability of the disease to medical management. Usually, the case is one in which numerous devastating exacerbations have occurred and during remissions, the patient never quite regains enough stamina to return to average activities and usefulness. Regrettably, it is the acute and severe exacerbation that brings forth a call to the surgeon. Far too often, he is expected to institute ileostomy in the practically moribund case, and as a result, the outcome is sometimes unsuccessful.

The indications for surgery commonly are listed as follows:

1. Chronic ulcerative colitis with advanced constitutional and visceral changes.
2. Irreversible polypoid degeneration and carcinoma.
3. Non-healing anorectal complications.
4. Obstruction and tumor mass; tubular stricture with impending obstruction.
5. Perforation, abscess and fistula.
6. Segmental ulcerative colitis.
7. Selected cases of recurrent and lengthy exacerbations of hemorrhage.

Many cases will usually fit into the first category and it is in this group that we would most emphatically urge the participation and supervision by the surgeon even though the disease be in a state of remission. It is here that early ileostomy and colectomy best offer the opportunity for overcoming invalidism and long-standing suffering.

Space does not provide for a full discussion of the remaining indications but as a rule they are uncommon and when present must be carefully evaluated by the surgeon. Abscesses should be drained and obstruction relieved. Pseudopolypoid change, in itself, we do not consider provocative of carcinoma unless the condition has been in existence for one or more years. This type of alteration is often reversible under successful medical regimen. Repeated proctoscopic and roentgenologic examinations are indicated, and should the polyps persist or increase, surgery must be instituted.

The need for surgery in the management of idiopathic ulcerative colitis continues to undergo fluctuation. Lowered mortality rates and the development of improved methods of ileostomy care, more than anything else, have reduced objections to operative interference. On the other hand, improved methods of medical management based upon the employment of newer drugs and advances in nutrition, have caused hesitation on the part of many physicians caring for the more seriously ill patients. Many other workers extol the values of modern psychotherapy.

As yet, no one method or combination of methods in medical management have proven universally successful. Advanced intractable forms of the disease continue to come to surgery. In this group, surgical supervision is indicated early in management and it is only through such supervision that opportune decisions can be made and success achieved. An all important product of this plan is the development of a close surgeon-patient relationship. Each step in management must be measured by the individual patient's progress and despite the many scientific methods available in our laboratories today, the decision to operate and the timing of stages must largely rest upon the surgeon's judgment. This, in turn, is based upon his thorough understanding of the patient. It is impossible to set down hard and fast routines, and outlined regimens are almost always subject to change. Rarely can an experienced surgeon employ his knowledge to the best advantage until he has all but lived with these seriously ill patients.

Preoperative Preparation

Perhaps the most important single consideration in the preparation of the patient with ulcerative colitis is nutrition. It is rare to find a satisfactory state of tissue and fluid protein in any of the more advanced cases. Usually a chronic deficit has existed for months and even years preceding operation. Evaluation of the nutritional status is difficult inasmuch as serum protein values may approach normal and even hemoglobin determinations may reflect but a mild degree of anemia. Yet, upon clinical appraisal an absence of subcutaneous resilience and muscle body is apparent. The skin is loose and lacks elasticity. Limbs are lean and breasts flat. The low status of protein reserves is at once evident. We are unable to accurately assess the amount of protein loss in exact terms of grams per kilogram of body weight or in other specific values, and we must restore protein in quantities commensurate with what general values we can determine through available laboratory and clinical methods.

The first phase in preparation is concerned with restoring normal red cell and hemoglobin values. This is best done by multiple blood infusions. Serum protein values will rise as a result of this therapy, but there will be but slow restoration of protein reserves. Blood infusions are continued until the circulating blood volume approaches normal. Circulating blood volume determinations are readily performed and the technic is simple enough to permit its adoption by any hospital laboratory[13].

High protein feedings are supplied preferably by the oral route, but intravenous alimentation as a supplement is rapidly becoming of greater importance than has been hitherto apparent. Invariably, these patients are resistant to accepting, by

oral intake, the large amounts of food materials required to provide necessary calories and protein. Appetites are poor, and in many cases, patients have habitually limited their dietary intake as a preventive measure against diarrhea. In other cases, previously prescribed, low residue diets, which have been followed for many months or years, have resulted in a strong distaste for these foods, and eating has become more of a burden than an enjoyment. Hence, it is with considerable difficulty that high protein nourishment is established. Certain modes of circumventing these difficulties are presented, but before discussing these, it is important that methods of estimating, in general, the protein requirement be established in order that dietary changes may be arranged to provide maximum improvement. Further, there must be a definite goal by which to judge the optimal timing for operative intervention. The most practical method for making these evaluations involves ascertaining nitrogen balance from day to day. Nitrogen losses in stool and urine are determined and compared to the amounts of nitrogen intake. When losses equal intake, a state of equilibrium is reached; positive balance is obtained when the intake is greater than the loss. It is very necessary that positive nitrogen balance be reached and continued until losses increase and equilibrium results. Nitrogen balance is then corrected and surgery can be considered.

Patients are weighed daily and frequent determinations of the circulating blood volume, circulating plasma volume, and circulating blood protein values, are obtained. Rarely does the patient reach a state of nutritional perfection, but it is usually not too difficult to render the subject safe for operation, providing, of course, that no complications arise requiring emergency interference.

High protein intake is best provided by supplementing a high protein, high caloric, diet by frequent liquid feedings of carbohydrate and protein hydrolysate or amino acid preparations. From 3,000 to 4,000 calories per 24 hours are necessary and protein intake should reach 250 to 300 grams in the same period. Should all efforts to supply these foods through the voluntary effort of the patient fail, tube feedings can be resorted to. We have employed a latex type of rubber tube made by weighting one end of a section of ⅜ inch penrose drain tube with 1 c.c. of mercury and allowing this to descend to the fundus of the stomach. Once every hour, ten or fifteen times a day, 200 c.c. of a tube feeding preparation, consisting of 20 grams of protein and an equal amount of simple carbohydrate such as dextrimaltose, is instilled slowly through the tube.

Intravenous supplementation is often instituted particularly where veins are easily accessible. The chief problem in this type of alimentation has been the furnishing of adequate calories with the amino acid or protein hydrolysate preparation used. Rice[15,16] has recommended the administration of 6 per cent alcohol, to accompany the amino acids or protein hydrolysate, and 5 per cent glucose. Alcohol is high in its caloric yield (7 calories per gram) and also possesses a desirable sedative effect. We have employed such alcohol, protein, and glucose mixtures to advantage in these patients.

A second important phase in preoperative preparation consists in the restoration of chemical and fluid balance. With the increased fluid intake, provided by

high protein diet, balance is quickly reached. However, electrolytes must often be furnished in larger amounts than might be expected. Frequent chloride, sodium, and potassium serum evaluation, are requisites. Serum carbon dioxide determinations are also of much value. A high sodium intake is advisable, and intravenous electrolytes are necessary, should frequent watery stools increase depletion.

The use of antibiotics for destroying bacteria in the intestinal tract is routinely employed in our patients. Sulfathalidine has been the most common drug used and we have found it to be remarkably effective in reducing colonic flora. Streptomycin, orally, is routinely administered forty-eight hours prior to surgery. Recently, chloromycetin, aureomycin, and terramycin have been used with excellent results.

A Miller-Abbott tube is passed into the upper small intestine just prior to operation. During the procedure, it can be advanced to the ileum. The tube causes some telescoping of the small intestine and greatly aids in retraction.

Choice of Operative Procedure

Colectomy, preceded by ileostomy, is the procedure which has most often provided the greatest benefit to the medically intractable case of idiopathic ulcerative colitis. Ileostomy, in itself, is rarely sufficient. The expectation that an ileostomy may be safely closed and intestinal continuity re-established is poorly grounded. Occasionally successful are attempts to eliminate an abdominal stoma by ileosigmoidostomy or ileorectostomy. However, for the most part these are only applicable in a very few, well chosen, cases. Indeed, as a part of our criterion for such a maneuver, the rectum must never have evidenced involvement by the disease. Such a qualification is rarely found and when we do find it, the chances are we are dealing with a segmental form of the entity and in such a case re-establishment of the bowel continuity is commonly acceptable. We have had no experience with transplanting the ileum to the anus after the method of Ravitch[17].

Primary colectomy and ileostomy is an acceptable operation but should be restricted to selected cases. On the other hand, we feel that to prolong colectomy beyond three stages is unnecessary.

Postoperative Care

With but few exceptions, it is uncommon to find other postoperative surgical patients requiring quite the same degree of close attention and exacting care which ileostomy patients demand. Daily laboratory studies are requisite. Efficient nursing is mandatory, and each change in temperature, pulse, and blood pressure must be accounted for. The early restoration and maintenance of electrolyte and fluid balance are all important. In the immediate postoperative period, the intravenous route for supplying electrolytes, fluids, and nutrition is unequaled. Fluid electrolytes and blood losses are replaced. Fluid and electrolyte losses through intubation are similarly replaced, but serious problems seldom develop prior to the full recovery and return in function of the intestinal tract. Early profuse discharge from the ileostomy is characteristic and within a few days 24 hour losses may approach 5,000 c.c. to 7,000 c.c. This fluid is high in electrolyte content being especially prominent in sodium ions. To compensate for this loss, intravenous infusions of

saline, Ringer's, Hartmann's, and lactate solutions are employed. Darrow's solution will aid in potassium replacement. Oral feedings are instituted early and consist of low residue and mostly liquid nutriments.

Laboratory data must consist of almost daily serum chloride, serum sodium, and serum carbon dioxide determinations. When stabilization is approached, chloride estimations may be obtained by daily urine tests and the other studies are provided less frequently. Potassium appraisals are important, but in our experience, prolonged and profuse electrolyte loss takes place before significant reductions in this ion occur. The routine circulating blood volume determinations are continued and nitrogen evaluations calculated in order that protein alimentation may be gauged to produce positive balance early in management.

Intramuscular penicillin and streptomycin are routinely administered until all dangers of sepsis have been surpassed. Aureomycin, chloromycetin, and terramycin are held in reserve to combat complicating infection resistant to penicillin and streptomycin.

The patient generally responds much slower to postoperative management following initial ileostomy than following the stages of colectomy. At least three weeks of hospitalization are needed for early convalescence. Complications are prone to occur in this period to the newly ileostomized patient and these must be anticipated.

There is seldom any excuse for the widespread skin excoriation occasionally seen in early ileostomy care. Prevention is most important and consists in the removal of all discharges as they are emitted. It is our practice to early apply some form of bag or container to collect drainage. In many cases it is practical to employ a Rutzen bag or similar receptacle within a few days postoperatively. A large square or circular sheet of rubber dam with a central opening for the stoma is quite convenient and efficient. Absorbent pads placed in the dam can be changed readily when soiled. Protective ointments of kaolin, zinc oxide, and petrolatum are of value and in many instances, kaolin dusting powder is sufficient. Tincture of benzoin, painted on the skin and reinforced by sprinkling with aluminum powder, occasionally produces a resistant barrier to erosion.

Statistics

In a personal series of 269 cases of chronic idiopathic ulcerative colitis, 54 patients (20.08 per cent) underwent operative intervention. In this group the following procedures were carried out:

TABLE I

	No. of Operations	*Deaths*	*Mortality*
Ileostomy	34	4	11.7%
Ileosigmoidostomy	3	0	0
Colectomy	27	0	0
Abdominoperineal excision	19	0	0
Miles excision (carcinoma)	1	0	0
Hartmann excision (carcinoma)	1	0	0
Closure of Ileostomy	1	0	0
Miscellaneous	18	0	0
Total	104	4	3.8%

Rehabilitation was most satisfactory in this group. In the patients undergoing colectomy 24 or 88.8 per cent have returned to active pursuits and normal life. One* patient is hospitalized, but convalescing satisfactorily following a recent colectomy. A young married woman who underwent ileostomy and a two-stage colectomy with removal of the diseased rectum has just terminated a successful gestation and is the mother of a healthy baby boy.

Summary

1. A brief historical outline of surgery in chronic ulcerative colitis is presented.

2. Early supervision in the medically intractable case is emphasized.

3. The indications for surgical intervention are discussed.

4. Nutrition is stressed as being the most important single consideration in preoperative management.

5. Ileostomy and a two-stage colectomy is the operation of choice for most cases.

6. In postoperative care the restoration of electrolytes is of most significance inasmuch as from 5,000 to 7,000 c.c. of fluid high in sodium may be eliminated daily from the ileostomy.

7. Three weeks hospitalization for the postoperative ileostomy patient is the minimal time necessary for observation and anticipation of possible complications.

8. Twenty-three colectomies are reported with a rehabilitation rate of 82.6 per cent.

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Discussion

Dr. Scudder Winslow (New York, N. Y.):—I congratulate Dr. Bacon and Dr. Trimpi for their fascinating story, unfolding the struggle this unusual disease has presented to the surgeon down through the decades, showing us the coming and going of surgical fads, and yet, with the passing of each decade, a gradual rise in the rehabilitation rate of these patients. There are few diseases that have and continue to present such a challenge to so many, the psychiatrist, the nutritionist, the surgeon, the medical man, of course, the surgical supply houses, the nursing staff, the house staff, and, last but not least, the loan department of the banks.

It takes the combined efforts of this large group, to give the surgeon nowadays the high rehabilitation rate that Dr. Bacon and Dr. Trimpi have approached.

In reference to Dr. Lilienthal's case of colectomy in 1899, Dr. Cave tells me that Dr. Lilienthal himself witnessed the autopsy in this city of that patient, a few years ago. She lived to sixty-six. She died of heart disease, and he had performed an end-to-end anastomosis between the ileum and distal sigmoid bowel.

I want to emphasize the point that Dr. Trimpi brought out, which we have found so frequently, and that is ileostomy is held out as a last resort to these patients after all else has failed. We get so enthusiastic and hopeful about each new antibiotic, and, after they have all failed, the surgeon is requested to perform an ileostomy which could be simple, but it approaches heroic surgery in some of these moribund cases, with a very high mortality rate.

To digress a moment, we were impressed in going over our emergency ileostomies, which carried a mortality rate of over 50 per cent. When we opened the peritoneal cavity to do our emergency ileostomy the peritoneal cavity was clean. At postmortem in these cases invariably the bowel went on to perforation and peritonitis; so, being on the radical side, in some of these selected cases we went ahead and performed an emergency ileostomy and colectomy in one stage. We have done this in five cases, with no deaths. These are quite dramatic cases, but it takes not only copious amounts of blood, expert anesthesia, but real teamwork, and we find those patients have done very well.

Dr. Bacon and Dr. Trimpi bring out one point that we find does occur so frequently, that in the distal diseased segment which is left behind after we have done our primary colectomy, and ileostomy, the patients gain weight, forty or fifty pounds, and are back at school or their vocation, and we forget about the distal diseased segment, and we have been seeing more and more carcinoma developing.

We have hoped always to try to save that distal segment and hook these patients back up and not doom them to permanent ileostomy. We have followed all of these rectums along and hooked up some of them, performing ileosigmoidostomy in six cases, two of which are successful. In the rest of these cases the disease has traveled up by contact, from the small bowel right up to the duodenum, and we have had to unhook them, resect considerable amounts of small bowel,

re-establish ileostomy and, as a desperate attempt, in three or four cases Dr. Cave and I have done vagotomies with success, but those cases are too recent truly to evaluate them; consequently we are doing as Dr. Trimpi pointed out, more and more abdominoperineal resections.

There is one thing I should like to mention. With all the magnificent new intravenous amino acids, vitamins, and the antibiotics, the single therapeutic agent that helps us the most is whole blood and frequent whole blood transfusion. As was pointed out, you will be fooled so frequently by routine hemoglobin, red blood cell and total protein studies. You must do blood volume studies to truly evaluate these laboratory procedures.

One thing that has helped us a great deal, as Dr. Trimpi has pointed out, is a polyethylene tube. Most of these patients who come to the operating room, have very poor veins. They are the bane of the house staff. Their veins are all used up, and we will not take these patients to the operating room until the polyethylene tube is in the jugular or cephalic vein.

The Miller-Abbott tube is very helpful. You get beautiful exposure; however, we feel that a desperately ill patient, one who is septic, edematous, and very weak cannot tolerate the Miller-Abbott tube.

Another great weapon in our armamentarium is intravenous alcohol. Those patients who are pouring forth ileal contents, losing electrolytes rapidly, becoming cold, clammy, and shocked (and they can do that in just a few minutes) intravenous alcohol has been of great help. A solution of 75 or 100 c.c. of alcohol in a 1,000 c.c. saline solution dramatically changes the picture in a few minutes. We believe this has saved several of our patients.

In closing I should like to re-emphasize the importance of ileostomy care. This is perhaps the most important responsibility that befalls the surgeon who takes care of these patients. The surgery is relatively simple. The great skill is the skill of the surgeon who works with the patient who has just been given an ileostomy. The surgeon and the patient tirelessly working together over this difficult handicap and seeing them through to the point where ileostomy care is a minimal factor. These newer bags with skin cement are magnificent. Ileostomy care, I might add, does begin in the operating room, in the formation of the ileostomy.

Recently before operation we have stood these patients up and, with indelible ink drawn out the best site for the ileostomy. The value of this has been great because sometimes with the patient lying on the operating table, one will get the ileostomy too close to the anterior-superior spine, the umbilicus, or the costal margin.

I know of no disease condition, as Dr. Bacon points out, in which it is more important that the surgeon play the role of psychiatrist, friend, and family counselor.

Dr. Charles B. Ripstein (Brooklyn, N. Y.):—I think Dr. Trimpi must be congratulated on a very thorough and complete résumé of the surgical efforts in this disease, and I think he is right in emphasizing that very few cases really

should come to the surgeon, but those which do are the very bad ones, patients who are toxic, almost moribund, or those who have intractable symptoms and have reached a state of cachexia.

About twelve years ago Dr. Gavin Miller, of Montreal, performed a resection for ulcerative colitis, and that was sort of an accident. He opened a patient to do an ileostomy and found that the entire ascending colon was almost gangrenous. He felt that to leave such a thing behind with an ileostomy was almost certain to doom the patient, so he carried out a primary resection of the bowel.

This was regarded as a horrible thing, although there had been a few resections performed in the distant past; however, the patient did extremely well, the course was very much better than the ordinary course of an ileostomy patient, and since we had all been so very much dissatisfied with the results of ileostomy, we started to wonder about it.

Why should a colectomy in a practically moribund patient do better than an ileostomy? Dr. Miller hypothesized at that time the reason why, but it took several years and the advent of the antibiotics before we had enough courage to try it as a planned procedure. With the advent of the sulfonamides and streptomycin and penicillin in the last five years, Dr. Miller, Dr. Campbell Gardner, and myself, working independently in different hospitals, have pooled our results and have now operated on about sixty cases of ulcerative colitis in the acute stage and in the very severe chronic stage, and have performed primary resection of the colon right down to the sigmoid, and in two cases we have done the complete job with a two-team abdominoperineal.

We feel that last is a bit of a stunt and rarely is indicated. There have been three deaths in this series of cases, which is a lot better than ileostomy alone ever gave. The interesting thing is that all of those deaths occurred in patients who had had the distal segment left in and in whom the distal segment had perforated, and in one case the patient had a massive hemorrhage from it in the postoperative period.

The strange thing was that the formidable operative procedure in these desperate cases didn't seem to kill them, and we have felt, going back over the cases, that the people didn't die from the operation but later, as Dr. Winslow pointed out, many of them had perforations and died of peritonitis, and others died because in a depleted patient, with hypoproteinemia and blood loss from the diseased bowel, and toxic absorption from the bowel left in situ, the added fluid and electrolyte loss from ileostomy in the first few postoperative days killed them, and it was utterly impossible to replace the blood, because they were losing 150 to 200 grams of protein a day, and we couldn't replace that.

I think the results of primary colectomy have proven themselves, and I am very glad to see that Dr. Trimpi has had as excellent and competent results as we have with this type of operation. I think that it represents a real advance in the surgical treatment of ulcerative colitis.

Dr. Howard D. Trimpi (Philadelphia, Pa.):—I want to thank Dr. Winslow and Dr. Ripstein for their excellent comments. Both of these surgeons have spoken favorably concerning surgical intervention in the fulminating case. There are many workers who feel that surgery should be postponed, but it is our experience that operation can prove to be a life saving measure in most of these very ill patients.

THE DIAGNOSIS OF COLONIC STASIS*†

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Essentially, habitual constipation is a derangement of the propulsive mechanism of the colon. The causes for this disturbance are manifold. They have been adequately discussed in the literature and no attempt will be made to evaluate them in this paper. Our investigation is limited to the roentgenographic study of the altered colonic motor function in individuals complaining of "constipation".

The realization that constipation is a form of stasis which may affect isolated portions of the colon has gradually evolved. Hurst[1,2] was one of the early investigators to develop such an understanding. He divided his cases into two types. One he called colonic constipation—designating an abnormally slow emptying of the colon and the other he termed dyschesia, meaning rectal retention. Many clinicians have used the term, colonic stasis, loosely, in preference to the word "constipation". However, it was only by adequate roentgenographic studies that a more understandable classification of this affliction has finally been established. Fantus[3] advocated the use of the term, colonic stasis, exclusively, because it designated a "real retention of bowel contents in some portion of the colon". Depending on what section of the colon, the residue was retained for an abnormal length of time, such terms as "cecal stasis", "proximal colon stasis", "transverse colon stasis", "rectal stasis", etc., were used. Buckstein[4] and others have also adopted similar groupings.

However, these classifications have not been uniform, no definite incidence of each type of stasis has been established, nor has their relationship to proper therapy been fully exploited. This investigation has been undertaken with the purpose of evaluating these factors. Another objective was to determine the efficacy of the common measures employed to induce bowel evacuation.

Selection of Cases

All the individuals investigated were selected from the gastrointestinal outpatient department. They were all ambulatory and their chief complaint was "chronic constipation". Care was taken in all instances to rule out organic disease as a possible etiologic factor. In addition, proper dietary habits were instituted and cessation of the use of laxatives were required before the investigation was started. The study was limited to chronic functional colonic stasis. Fifty patients were observed, their ages ranged from 24 to 83 years. The majority were over 40 years.

Method of Study

Each case was investigated as follows: The day the study was started, the individual was instructed to evacuate his bowels by enema. This precaution was

*Read before the Fifteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 9, 10, 11 October 1950.

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This study was aided by a grant from G. D. Searle & Co.

necessary so as to avoid the possibility of fecal impaction, especially in the older age group. An average dose of flavored barium sulphate in water was administered orally. The patient was instructed not to take any cathartic or enema after this and to stay on a normal diet. Fluoroscopic observations were then made at twenty-four or forty-eight hour intervals until no more contrast medium was seen in the gastrointestinal tract. The emptying of the various segments of the colon as well as the total emptying time was noted and the type of stasis recorded. Following this, the patient was again evacuated by enema.

In order to determine whether the dysfunction of the colon remains constant, repeated studies were conducted in some of our more interesting cases. In most instances, the same type of delay of segmental colonic motility as originally observed was found. In an occasional patient, the original pattern was slightly altered. Two of our cases were exposed to three such investigations with the same result. Most of the individuals studied were under our care for several months. We can assume from our observations that colonic stasis conforms to a given pattern which tends to remain more or less constant in the same individual.

Classification

The standard division of "constipation" into the spastic and atonic varieties is not justifiable. The diagnosis of these entities are based chiefly on roentgenographic impressions. Clinically, the character of the stool may also be a contributing diagnostic factor. Such a diagnosis largely depends on the number and the degree of contraction of the haustra markings and secondarily on the width of the lumen. There is no reliable method for measuring either. That spasm of the colon may take place from time to time has frequently been observed fluoroscopically during the administration of a barium enema and occasionally during sigmoidoscopy. These contractions are transient, lasting only a few seconds to minutes. Almy and his associates[5,6] have recently demonstrated spasm and engorgement of the mucosa of the sigmoid during "emotional tension". These phenomena were recorded in individuals with and without "constipation". The inference that spasm of the sigmoid may be prolonged enough to be the major cause for colonic retention of many years' duration is open to conjecture. It is conceivable that it may cause stasis for short periods of time in some individuals. However, it is more probable that such contractions are reflex reactions to intrinsic or extrinsic causes and that they may give rise to pain and discomfort similar in character to those that take place in other parts of the gastrointestinal tract. The term "atonic constipation" is also misleading. Atony of the colon is uncommon and if demonstrated at all is usually found in one section of the bowel and is often accompanied by spasticity in some other segment. Furthermore, "spasticity" or "atony" is frequently observed in individuals having normal bowel habit and even in diarrheas. It can readily be seen that no clear understanding of the delayed bowel function can be obtained from such a classification. When such entities as spasticity or atony are observed, they should be considered as contributory rather than the major etiologic factors.

Our classification is largely dependent on knowing in which segment of the colon the residue is retained for an unusual length of time. This was determined by daily fluoroscopic observations.

Three basic patterns of abnormal retentions have been identified. Retention in the cecum or ascending colon is called proximal colon stasis. When it occurs in the transverse and/or descending colon, it is termed distal colon stasis and when it occurs in the rectum it is called rectal stasis. In addition to these three fundamental types, occasionally, we may observe any combination of the above.

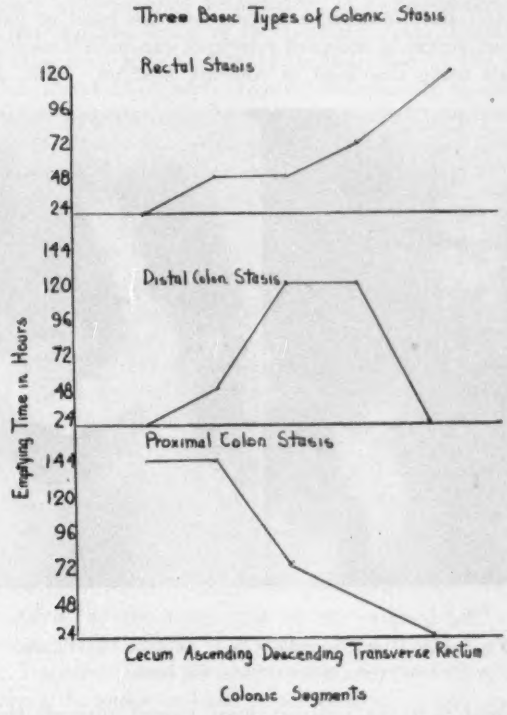

Fig. 1

These are designated as combined colon stasis. Another variety which may be encountered is imaginary constipation and this is characterized as pseudostasis. As a result, colonic stasis has been divided into (Fig. 1):

1. Proximal colon stasis.
2. Distal colon stasis.
3. Rectal stasis (dyschesia).
4. Combined stasis.
5. Pseudostasis (coprostasiaphobia).

Normal Emptying Time of the Colon

Many methods have been used to measure the time required for material to pass through the intestinal tract. Einhorn used beads, Barnett—millet seeds, Alvarez and Friedlander—capsules, Mullinos—carmine dye[7], etc. Although these studies gave us information regarding the total emptying time, they could not designate the faulty portion of the gastrointestinal tract involved in abnormal cases. Knowledge of the time it takes for food residue to pass through the colonic segments is largely dependent on roentgen observations. Although there is no fixed rule as to the exact time it takes a barium contrast meal to pass through the normal colon, some generally accepted principles can be followed. According to a survey of normals using this kind of contrast medium, Todd, Hurst, Wallace

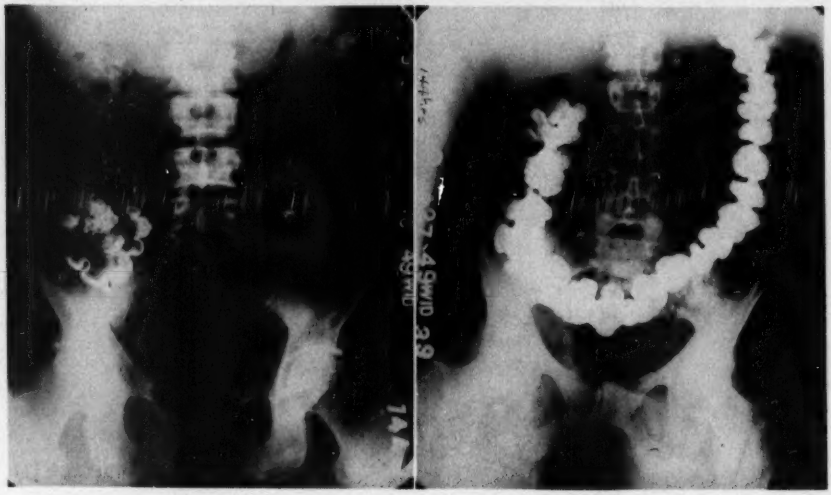

Fig. 2 Fig. 3

Fig. 2—Cecal and ascending colon retention, 144 hours.
Fig. 3—Transverse colon retention, 144 hours.

and others[8] showed that the contrast meal moved through the colon at an approximate given rate, arriving at the cecum in 4½ hours, hepatic flexure at 6½ hours, splenic flexure at 9 hours, etc. Little emphasis was placed on the emptying time of the segments. However, Fantus, Kopstein and Schmidt[9] observed that 92.8 per cent of their series had an "optimal cecal emptying time" of 24 hours, the remainder emptying in 48 hours. Marked variations existed in the "total emptying time", the majority being 48 to 72 hours. Kantor[10], in an independent study, also felt that an emptying time of the colon over 72 hours was abnormal. With the above as a normal standard for emptying, retention over 72 hours in any segment of the colon has been classified as abnormal.

Type of Colonic Stasis

1. *Proximal Colon Stasis:*—Apparently, the motor function of the proximal colon is different from the remainder of the large intestine. It is innervated by the motor fibres of the vagus, whereas the remainder of the colon is supplied through the pelvic nerves[11]. Furthermore, it is the only portion of the colon where antiperistaltic waves have been demonstrated. Retention in this part of the colon may either be confined to the cecum alone or it may include the ascending and at times the first portion of the transverse colon. It may be assumed that such a disturbance is indicative of a dysfunction of the alternate propulsive and retropulsive action of the proximal colon. Cannon[15] was first to report antiperistaltic movements in the proximal colon of the cat. Evidence of similar peristaltic waves have been recorded occasionally in man. Retention of the residue in this segment from 24 to 48 hours has been considered normal. Abnormal retentions of 144 hours was observed in our case. This class of stasis is not common, the incidence in our series was 2 per cent (Fig. 2).

2. *Distal Colon Stasis:*—This form may involve the transverse, descending colon and pelvic colon. It is apparently caused by a lack of the initiation of the mass movements which propels the fecal mass into the rectum. Actual propulsion of the fecal mass through the distal colon into the rectum is accomplished by sudden mass movements originally described by Holtzknecht[12]. These last only a few seconds and occur several times in twenty-four hours. These mass movements start at the hepatic flexure and may be initiated by the gastrocolic reflex. This takes place when sufficient food is ingested to cause distention of the stomach walls. Abnormal retention of the residue in this portion of the colon from 96 to 168 hours has been observed in our investigation. This seems to be the most common type. In this study, almost half (48 per cent) had it (Figs. 3 and 4).

3. *Rectal Stasis (dyschesia):*—This type was originally described by Hurst[1,2]. Normally, the rectum is empty. When the fecal residue is forced into the rectum by a mass movement, it causes it to distend. The stretching of the rectal walls stimulates sensory nerves and produces an urge to defecate. This desire usually is voluntarily delayed by the contraction of the external and sphincter muscles until a suitable time for defecation is available. Finally, when this occurs, evacuation takes place. Intraabdominal pressure is increased by holding the breath which fixes the diaphragm, the abdominal and pelvic muscles contract and anal sphincters relax, resulting in defecation. When the individual neglects to respond to the urge to defecate, the rectal sensory threshold is raised. The musculature gradually adapts itself to a large volume of feces and eventually very considerable accumulation may occur. Dehydration of the fecal mass occurs slowly and defecation becomes more difficult. This may eventually lead to fecal impaction. As a result of the existing stasis, gradual dilatation and lengthening of the rectum occurs. In our cases, abnormal rectal retention has been observed to exist from 72-144 hours without the individual having any desire to defecate. The incidence of this variety was 16 per cent in our series. This conforms to Kantor's[13] 18 per cent occurrence (Fig. 5).

4. *Combined Stasis:*—In one instance, colonic retention was observed to take place in both the proximal and distal colon, while transit through the rectum was apparently normal. A cecal emptying time of 120 hours and a distal colon retention of 144 hours was observed in the same individual. Another variety of this group was a case of distal rectal stasis, transit through the proximal colon being normal. Other combinations are possible. They are proximal rectal and proximal distal rectal types. Fortunately, the combined forms are uncommon, the incidence being 4 per cent in our series.

5. *Pseudostasis:*—It is interesting to note that often a patient's complaint of "constipation" does not in all instances agree with the roentgen findings. The statement made by these individuals as to the number of days elapsed before they had a bowel movement usually did not correspond to roentgen observations.

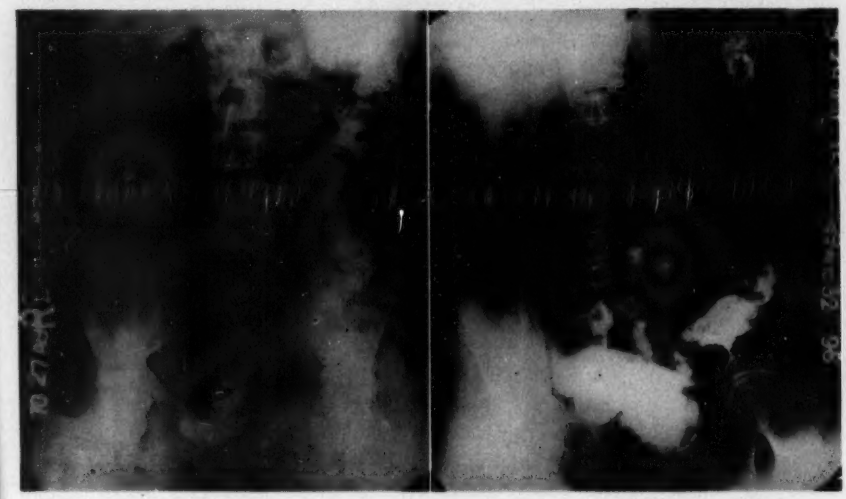

Fig. 4 Fig. 5

Fig. 4—Transverse and descending colon retention, 168 hours.
Fig. 5—Rectal retention, 96 hours.

There was a strong tendency for the patient to exaggerate his complaint. In this group, complaining of constipation, x-ray studies revealed no stasis in any part of the colon, their segmental as well as the total emptying time was within normal limits. These individuals were greatly disappointed when they were told that they were not constipated. Fantus[3] coined the word "coprostasiaphobia" as descriptive of such cases. This term implies a fear of not being able to have a normal bowel movement. It is important to emphasize that such entity as imaginary constipation exists and that its incidence is relatively high. As many as 30 per cent of our cases had this form of disturbance.

Clinically, it is difficult to distinguish the various types of colonic stasis, since the symptoms of the different varieties of retention are similar (Table I). How-

ever, rectal dyschesia may be elicited by rectal digital examination and a suspicion of pseudostasis should be aroused by the individual's predominant neurotic symptoms of tension, nervousness, tight headaches, etc.

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Discussion

Dr. William W. Lermann (Pittsburgh, Pa.):—I have been very much interested in hearing Dr. Barowsky's paper and wish to congratulate him on the work he has done. It is the type of work that is very much needed, for I believe that stasis or constipation leads to so many chronic ills that it should be the subject of more frequent papers and discussions at all gastrointestinal meetings.

When I first read Dr. Barowsky's paper, I was greatly interested in the title of it, as it is such an all-inclusive title; however, I seem to find it difficult to agree entirely with him on his interpretation of the excellent work he has done. His work is done on a group of patients taken from the gastrointestinal out-patient department, the majority were over forty years of age, up to eighty-three years of age, and I believe the group numbered about fifty. They were given barium by mouth, and fluoroscopic observations were made at twenty-four, forty-eight, and in some cases seventy-two hours, the entire study being confined to the colon.

These stasis cases were grouped as follows:

1. Proximal colon stasis (cecum or ascending colon).
2. Distal colon stasis (transverse or descending colon).
3. Rectal stasis (rectal retention).

He has very ably discussed the various types of stasis and quoted numerous authors. He has again affirmed the anatomic and physiologic function of the colon as has been done previously and, in the light of the many recent medical ad-

vances, this is always worthwhile. He has explained his treatment and has also suggested that our present nomenclature or standard division of constipation into the spastic and atonic varieties be changed and hereafter we speak of proximal, distal, and rectal stasis, and the term "combined colon stasis".

These observations, as I wish to emphasize again, are very excellent, but I do not believe that roentgen-ray studies alone (fluoroscopy and films), done at twenty-four, forty-eight, seventy-two, and ninety-six-hour intervals are sufficient to justify his title of "The Diagnosis of Colonic Stasis". To me this title is all-inclusive, but it is quite different from the body of the paper, which discusses only a limited study, by x-ray alone, of the problem. If this paper were titled "Roentgen-Ray Observation of Colonic Stasis", it would be an excellent paper.

To my way of thinking, there are so many factors in this problem that no one can explain stasis fully by x-ray findings of the colon at twenty-four, forty-eight, seventy-two and ninety-six-hour studies alone. Dr. Barowsky may not have found spastic constipation in his group of cases, but I assure you we do find a great many of these cases, particularly in the last few years. If this study did not confine itself to out-patient department cases, but included the busy, harassed, tired, overworked executive, industrialist, business and professional man, and so forth, I feel sure that the observations would be somewhat different.

When one considers the way in which all of us live these days, the personal problems, the financial problems and the many, never-ending problems inflicted upon the entire country in the last twenty years, I think we can rightly say the spastic colon is very prevalent.

Prior to 1932, for many years we saw numerous cases of atonic constipation. Today in our work we find atony in not more than one in one hundred to two hundred patients, and the rest come under the very distinct classification of spastic constipation. You could give it many other names, if you wished, and you could call it Roosevelt or Truman constipation, or Fair Deal or New Deal, or Twentieth Century constipation, but from my observation it has become a very serious problem, and cannot be thrown out merely as a contributing factor.

I feel sure a great many of us, when we listen to Mr. Truman and Mr. Ewing discuss the socialization of medicine, or read about their discussing it, get little twinges of spasticity down the descending colon, and perhaps little butterflies in our stomach. I am sure the steel men all do when the Government is discussing building new steel mills as the first step toward socialization of the steel industry.

These problems just cannot be thrown out the window; you just can't do it. They are definite problems, and I think that what we all have to do is treat the patient first, then the disease.

It is interesting to note that with this type of constipation there is not only a narrowing, but also a definite shortening of the colon, particularly the lower half, which is so well shown by comparing the twenty-four-hour film with a barium enema film. In addition to this, one must also consider many other factors, such as achlorhydria, hyperchlorhydria, chronic intestinal infection, cholecystitis, duodenitis, enteritis, and many associated stress-and-strain medical conditions,

as the muscular activity of the entire gastrointestinal tract cannot be disassociated. An x-ray observation of the colon alone does not permit conclusive enough evidence to justify the suggested change in the classification mentioned.

I don't see how it is possible to feel that what one finds in the colon is entirely the result of a colonic condition. I think we have to start at the beginning of the tract.

There is one thing in the treatment that Dr. Barowsky mentioned that was quite interesting to me, and that was the fact that the bulk did not help in the proximal stasis. As you all know, fecal material should be fluid until it reaches about the midtransverse colon. The cecum, I believe, is the only part of the body in which the fluid gastrointestinal contents run uphill. Perhaps adding the bulk to it may have a very definite mechanical effect in that special condition.

Again I wish to thank the doctor for his excellent paper. I am sorry I can't agree with the total interpretation. I personally am not at all ready to discard spastic constipation. I regard it more and more as the basic cause in the great majority of people who are subject today to all the many problems that come with living in this day and age.

Dr. Henry A. Monat (Washington, D. C.):—The papers read to us this morning actually describe the complaints of a majority of our patients. The complaint of constipation is not always as benign as it seems on the surface inasmuch as we deal with people who have used laxatives for a number of years.

The sigmoidoscopic evidence of this complaint shows definitely irritated mucosa with spasms. I feel that the definition of Dr. Barowsky's colonic stasis is a very good one inasmuch as spasm of the colon may be encountered in perfectly normal individuals at one time or another.

To treat a chronically irritated colon with more substances which tend to increase this irritation, is physiologically unsound. I feel that the less we do for these patients by way of medication, the sooner their colons will improve. The treatment should consist of re-education of the patient as to his dietary habits, his timing as to when to go to the toilet and rectal hygiene. The majority of these patients get well; some obstinate ones have to be seen quite frequently at the office and encouraged. Occasionally one has to resort to small enemas of half to one cup of hot water.

In all these years of treating constipation, this method has proved very effective.

Dr. Horace W. Soper (St. Louis, Mo.):—I must say a few words on this subject.

For many years I have used the carmine 5-grain capsule, two of them with the evening meal. Under normal conditions the stool following this will contain a slight amount of the carmine, and the second evacuation, on the next day, the entire stool must be colored with it. On the third, a few slight streaks are there. That is normal, and that is a very good test, a great deal better than the barium test, for it gives you the time in which evacuation occurs.

Now, the doctor didn't like the term "atonic colon", but the barium enema will sometimes show an entire colon and that is enlarged all the way through, including the ileum and the sigmoid, all enlarged. There is one treatment for that that I have found and have used for forty years or more, and that is Parke, Davis & Company's straight fluid extract of Cascara, given before each meal, the patient regulating the dosage as time goes on.

I have seen those colons get smaller. I have seen them have normal evacuations in time; however, there is another type where the entire colon seems to be atonic excepting in the iliac and sigmoid portions. In your physical examination you can always feel for that spastic iliac. You can feel it when it is there, and there is one treatment for that, which is effective, and that is the nightly use of the mineral oil enema. Some colitis is usually present there. Mineral oil is not a culture medium; it tends to relax the spastic portion. It goes clear up to the cecum, and within one hour, as we have determined in our experiments, by adding barium or bismuth to the oil—it reached the cecum. It is retained all night. It discourages the growth of all bacteria.

The mineral oil enema is furthermore absolutely curative in many conditions. In early ulcerative colitis it is curative. The mineral oil enema—a retention enema —is also curative in diverticulosis. I have many slides which show complete disappearance after a good long course of the mineral oil enemas, where the entire colon was involved in the diverticulosis.

Dr. Harry Barowsky (New York, N. Y.):—I want to thank Dr. Lermann and the other discussers for their interesting comments. I appreciate their remarks.

I agree that the roentgenographic method of observation of these forms of colonic stasis is a limited form of investigation, but it is a fairly accurate objective method and any type of investigation which would enhance our knowledge on this subject is a valuable contribution.

There is no question in any of our minds that spasticity exists. I think we all accept that. Anyone with experience has seen spasm of the colon fluoroscopically with the barium enema and on sigmoidoscopic examination, but the interpretation as to the significance of the degree of spasm is very evasive; it is merely an impression that the individual gets by examining his x-ray films.

I also want to emphasize that many cases with normal bowel movements, have spasm; and even, in patients with diarrhea, we have observed marked spasm of the sigmoid.

Spasticity of the colon may be an etiologic factor in some individuals, having chronic constipation. However, it plays a secondary rather than a major role in such disturbance. If it is the cause, then constipation is usually of short duration, lasting only a few weeks or months. These cases respond to standard methods of management. However, the therapeutic response of our cases to general measures was poor. We selected the worst possible cases. Such individuals in all probability

have an altered motor function of the colon. This can best be evaluated by a roentgenographic method of observation, where segmental emptying time can best be demonstrated.

Other methods employed in the study of colon motility show the total emptying time but will not designate the specific segment involved in delayed emptying.

Again I want to thank the discussers, and I hope this paper will stimulate further interest in a much neglected subject.

GASTROSCOPIC BIOPSY
CORRELATION OF CLINICAL FINDINGS AND TISSUE BIOPSIES OF THE STOMACH*†

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The operating gastroscope was introduced by Benedict in June, 1949. This scope has been available to us since September of that year and since October it has been used routinely for all gastroscopic examinations. This eliminates the necessity of using two different scopes and is important because of the patient's objection to the procedure. We have performed ninety-one examinations and biopsies since then and have found the instrument to be very satisfactory in most

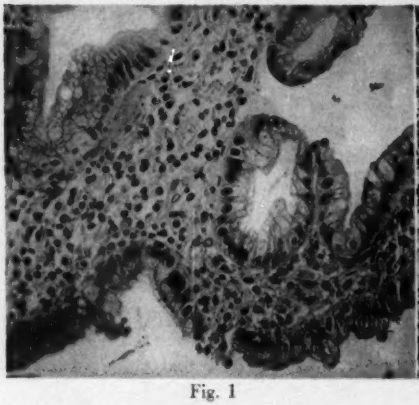

Fig. 1

Fig. 2

Fig. 1—High power—Normal gastric mucosa showing usual type cells found in interstitial tissue. Changes in thickness of glands due to cutting on bias.

Fig. 2—Normal mucosa with tendency to polypoid hypertrophia—increase in goblet cells. Normal interstitial tissue.

respects. The instrument is safe with careful use and the examination should be without hazard to the patient.

A good satisfactory examination is closely related to the conditions under which it is undertaken. An experienced examiner and a very relaxed, cooperative patient will result in a high degree of accuracy. Under ideal conditions such as these, mistakes will occur. They are mistakes of judgment, or of interpretation and, very often on the part of the gastroscopist, mistakes of omission. The reverse

*Read before the Fifteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 9, 10, 11 October 1950.

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of this situation is at times also true. We have seen an object in the stomach that appeared to answer the criteria of malignancy. Accordingly, operation was urged and at the operating table, the surgeon found a normal stomach. If the surgeon has not opened the stomach and looked inside, this may not be correct as Palmer has recently pointed out, showing 4 cases preoperatively diagnosed as carcinoma of the stomach with no operating table findings. All of these cases were subsequently re-operated upon and were found to have gastric carcinoma.

Some of these difficulties are eliminated by the flexible operating gastroscope. A biopsy showing malignant change is not open to the challenge that exists with the individual differences of visual image interpretation. A positive biopsy is an absolute and not a relative diagnosis and supersedes in importance all other parts of the clinical evaluation. A negative biopsy, on the other hand, must be accepted cautiously. It may mean only that the biopsy has not encountered the diseased portion of the stomach, it may mean that a diffuse disease does not exist, or it may mean that an ulcer is malignant on one side and benign on the other. A negative biopsy does not rule out such conditions. We very early learned that to see an ulcer was one thing but to direct the forceps of the operating gastroscope exactly into the edge of the ulcer or safely into the base of the ulcer was an action of a different kind. This was very often impossible technically.

We are convinced that biopsy through the flexible operating gastroscope is a practical and a worthwhile addition to our methods of examination. We feel that it should be used routinely and will eventually replace the older methods of examination. The procedure is safe and is without any more complication than simple gastroscopy. It is important to note that the patient has no discomfort or pain and he is not aware of the time when the biopsy is taken. No bleeding has occurred. In most cases the biopsy is observed until bleeding stops and this rarely takes longer than 30 seconds. The biopsies are immediately fixed in 10 per cent formalin solution and therefore show no autolytic process on the mucosa. If no gross or localized pathology is visualized, then from two to four random biopsies are taken, one or two from near the angulus and one or two from the body of the stomach, whichever is most accessible. We have been gratified to note the complete absence of digestive changes found in the gastric mucosa. Several pathologists who have inspected these slides have voluntarily commented on the fact that they have not previously encountered such clear specimens of the gastric mucosa. Rarely is there more than ten seconds elapsing between the time that the biopsy is taken and the time that it is fixed in solution. At some later date, we intend to more thoroughly study this question of tissue fixation using other solutions and comparing results.

We have previously given a report of the first 60 cases encountered in this group to which we are now adding an additional 31 cases. The statistics concerned include the entire 91 cases and are somewhat different as would be expected from the original group.

The diagnosis was reached in these cases on the accumulative evidence of all of the examinations. This included history, complete physical examination,

fluoroscopic and x-ray examination, gastric fractional, gastroscopic examination and the clinical conclusions after all information had been obtained. It may be that some of these cases will later develop pathology, but it is safe to assume that at this time, they did not have a recognizable existing disease pattern. The biopsies were all taken at random in the normal stomachs and an attempt was made to reach the various representative areas of the stomach. These biopsies have had multiple sections taken through all of the tissue obtained and all the sections have been examined in each case. Minor changes showing some atrophy, metaplasia, or glandular changes suggestive of irritative phenomena are very common in this group. They are so common that we have often wondered whether they signify an unknown state. We hope that after examining several hundred of these cases, a more clear-cut picture of the normal pattern will result. Certainly, at this time we cannot predict what the normal range of tissue is to be. These changes may be from chemical irritants, from localized irritation in the stomach,

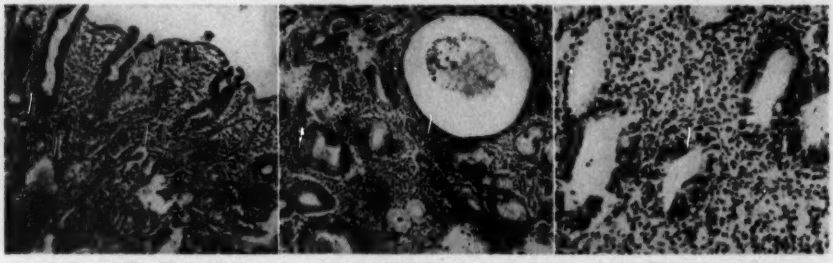

Fig. 3-a Fig. 3-b Fig. 3-c

Fig. 3-a—Low Power—Showing atrophy of mucosa—absence of superficial mucosa—no interstitial infiltration. Some evidence of glandular metaplasia.

Fig. 3-b—Low Power—Cystic change of one of the glands showing leucocytes and coagulated fibrin. Marked interstitial infiltration and irritative changes of some of glands. Can this be due to "actual inflammation" and not solely irritative?

Fig. 3-c—High power—Shows metaplasia of glandular elements. Are these changes very early malignancy?

or from allergies or thermal irritants, but just exactly what these are, we cannot say at present.

The following photomicrographs have been selected from only those cases showing a complete absence of gastric pathology. You will note the wide range of tissue that we have encountered. Several of these slides have at times been described as revealing gastritis. What is the type of gastritis it reveals? That is a question that we cannot answer because we also have been unable to classify gastritis and the changes that one may encounter within that group. This is a selected group of so-called normals and probably includes many types not classified at present that will eventually fit the pattern of gastritis.

Gastritis

The gastroscopic description of gastritis is a well-recognized pattern. The clinical story is often confusing and seldom fits into a recognizable pattern. It would appear that many of the individuals having gastritis by gastroscopic exam-

ination are also within the group of patients suffering from so-called gastric neuroses. Is there a connection between these two facts? Do they overlap and are certain of the gastritities that we are describing in actuality gastric neuroses with objective gross changes? These are questions that again we cannot answer but can theorize upon. Most roentgenologists, who have been experienced in conjunction with gastroscopic examination, are very loathe to make a diagnosis of gastritis by x-ray. To the gastroscopist, the reason for this is obvious. The so-called hypertrophic gastritis pattern, so well described by Schindler, with its cobblestone appearance presents in actuality a fairly smooth surface in silhouette and there is very little about it that would reveal itself on the x-ray plate or the fluoroscopic examination. It might even at times appear like atrophy because the rugal folds, by their edema and swelling, are eliminated and the valleys or depressions are not seen. The roentgenologist accordingly often asks for a gastroscopic examination and will be content to rest upon the report of the gastroscopist in regard to the gastric tissue. The gross appearance of most gastritities is well agreed

TABLE I

CARCINOMA CASES CLASSIFIED BY BRODER GRADE (MICROSCOPIC) AND BORRMANN CLASS (GASTROSCOPIC)

Case No.	Borrmann	Broder
1	IV	IV
2	IV	IV
3	III	III & IV
4	I	III & IV
5	II	II & III
6	III	III & IV
7	IV	IV
8	II	III & IV
9	III	IV

upon. Their characteristics are so well known that it will not be necessary to stop and describe them at this point. The accompanying group of photomicrographs were selected as representing true gastritis either hypertrophic, erosive, atrophic, or a hemorrhagic type. After studying all of the sections of these cases and after comparing them with the normal tissue previously described, we believe that this group of cases fits into the pattern of the gastritities but we also believe and agree with Dr. Benedict that "more study is needed in classifying gastritis as to type and severity". At present, we are unable to correlate our gastroscopic picture with the microscopic findings and again, as in the normal stomach, believe that a closely correlated study of several hundred well controlled cases is going to be needed before the microscopic picture of gastritis will be more clearly understood. We have been confused and our original opinion on the diagnosis of the gastritis from the gastroscopic point of view has often been temporized or changed by our resulting inspection of the tissue biopsy. In this regard there are several questionable terms that are used pathologically.

The group of cases generally discussed in gastritis would include atrophy. We fail to see where atrophy under the present pathological concept is concerned

with an inflammatory process which gastritis presumes itself to be. If, as Dr. Schindler has stated, atrophy is the end result of hypertrophy, then they are both one and the same pathological process and should be so described in our literature. Is hyperplasia of the mucosa of the stomach a true gastritis? Dermatologists often see hyperplastic changes of the skin but they do not classify this as a dermatitis. It seems to us that a microscopic description will eventually be correlated with a gastroscopic description making a more complete and a more accurate diagnosis in the overall evaluation of the case. In this regard, we have devised a master sheet which we are now having submitted for all patients before gastroscopy. This master sheet contains all of the relevant details of the case and when filed completely, would contain everything necessary for a complete protocol. With this information after several hundred biopsies have been taken and they have been compared with an equal number of normals we should be able to offer some sort

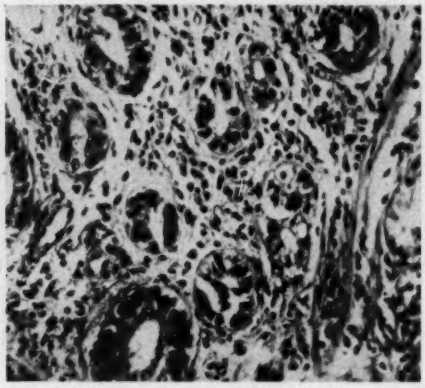

Fig. 4—High power—irritative changes—dark staining nuclei varying in position and relation to basement membrane. Some pyhnotic nuclei: Increase in interstitial round cells. Probably chronic gastritis.

of a classification that will be clinically and pathologically acceptable to the pathologist, the gastroscopist, the internist, and the surgeon. It seems to us that this is vitally necessary in order to eliminate much of the confusion of our present day terminology. With more individuals doing biopsies through the operating gastroscope and more tissue specimens accumulating, this eventuality should not be in the too distant future. We have decided that our cases should be classified as either normal mucosa or gastritis mucosa, not specifying the type. At some later study, type classification can be undertaken for purposes of clarifying the details.

Peptic Ulcer

Gastric ulcers can be accurately described and classified by x-ray. The gastroscopist adds his direct view of the ulcer and certain factors concerning the characteristics of the ulcer that cannot be seen by x-ray. If the gastroscopist can see the ulcer, his information should bring the accuracy of differential diagnosis to

about 95 per cent. This, of course, concerns the differential diagnosis between benign and malignant lesions. Very often the inexperienced gastroscopist will report upon a gastric ulcer only partially seen. This may be an ulcer seen in silhouette or the edge of an ulcer in the prepyloric region. These reports are not too safe to rely on for prognosis or final diagnosis. The gastroscopist should be the one that is first to point out this weakness in the examination.

The operating gastroscope is of value in these cases to a limited degree. First, we have found it technically very difficult to biopsy the gastric ulcer. Manipulation of the forceps and the aim of the examiner at such a distance from the ulcer are both very difficult. At first we were perturbed about the possibility of perforating the base of these ulcers, but in later examinations we have been able with great care to take a small section from the base of several of the gastric ulcers in

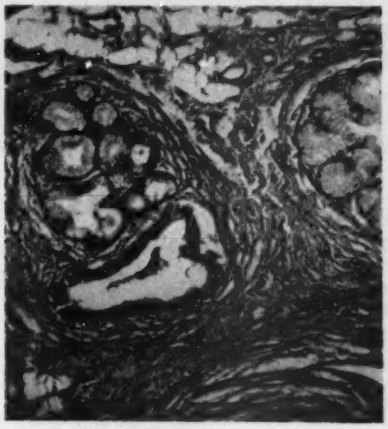

Fig. 5—High power—Case of stomach with actinomycosis from liver source and gastrohepatic ligament. Shows metaplasia of glandular elements next to normal ones. Some degenerative changes in interstitial tissue.

addition to a section at the junction of the base of the ulcer and gastric tissue. Ideally, we believe that one should attempt to get a section at the junction of the ulcer and the build-up of gastric tissue at the edge, and if possible, two biopsies should be taken, one on each side of the ulcer. We have also biopsied tissue from the stomach at some distance from the ulcer and are attempting to correlate this tissue with the normal and gastritis pictures we have previously shown. The stomach with a gastric ulcer is a diseased organ and the gastric ulcer may be a manifestation of a disease process throughout the stomach. Those cases we have encountered have appeared to show some variation of the mucosa but we are not ready to base any conclusions on our limited number of cases.

One must forever remember the carcinoma *in situ* of the gastric ulcer. Biopsy is no different than pathological section of the surgical specimen. One small corner or edge of any gastric ulcer may be malignant. It is, of course, impossible to biopsy

the entire ring of the ulcer. It might be pointed out that many pathologists do not section the entire ulcer. I believe that the one or two biopsies that are taken from the gastric ulcer by the operating gastroscope will, in the vast majority of cases, be as good as the few sections the pathologist removes from the surgical specimen of the stomach.

All but one of the ulcers that we have studied have been benign. Many of them have, for one reason or another, been removed surgically. This does not mean that our policy is that of removing surgically all gastric ulcers. If the stomach of the individual examined shows atrophic gastritis and gastric ulcer, a subtotal resection is done. If the edges of the ulcer are rolled and there is any evidence of edema or tissue build-up in the edge of the ulcer it is considered potentially malignant and a subtotal gastric resection is recommended. If, however, the ulcer is clean, shows a punched-out appearance and there is no atrophy of the stomach mucosa, it is considered a benign one and is treated medically for about three weeks. At the end of the three week period, the patient is re-examined by

TABLE II

RESUME OF CASES

Diagnosis	Cases	% of Total
Gastritis	25	27.4
Normal	20	21.9
Gastric Ulcer	13	14.2
Malignancy	9	1.9
Postoperative Stomach	7	1.7
Normal Stomach With Duodenal Ulcer	6	1.6
Gastric and Duodenal Ulcers	4	1.4
Marginal Ulcer	3	1.3
Gastric Polyp	2	1.2
Gastric Diverticulum	1	1.1
Polycythemia vera	1	1.1

gastroscope and x-ray. If the ulcer has not shown great evidence of healing at that time, the patient may be subjected to subtotal gastric resection. If, however, and this is true in most cases of benign gastric ulcer, the ulcer has healed and only a scar can be seen, the patient is sent home for a six weeks trial of limited activity. At the end of six weeks they are again examined by x-ray and possibly by gastroscopy and at that time our final conclusion is made on whether the patient will be subjected to surgery or continued as a medically treated case. We realize, of course, that gastric malignancies that ulcerate will show evidences of healing during this period of time but in our experience all of those ulcerations that were malignant have broken down within this nine week period. It is true that we may not have operated upon some of them as quickly as we should, but the mortality on this group of cases has been no worse than that of carcinoma of the stomach in general and perhaps somewhat better. We feel that we are, therefore, subjecting the patient to a calculated risk and that with complete patient cooperation the few cases with malignancy that ulcerate and then heal will still be operable at the end of this period.

Gastric Polyps

During the course of these examinations we have encountered two cases of gastric polyp; both of these have been well seen by the x-ray and were well visualized by the gastroscopist. Biopsies were taken from, as nearly as possible, the

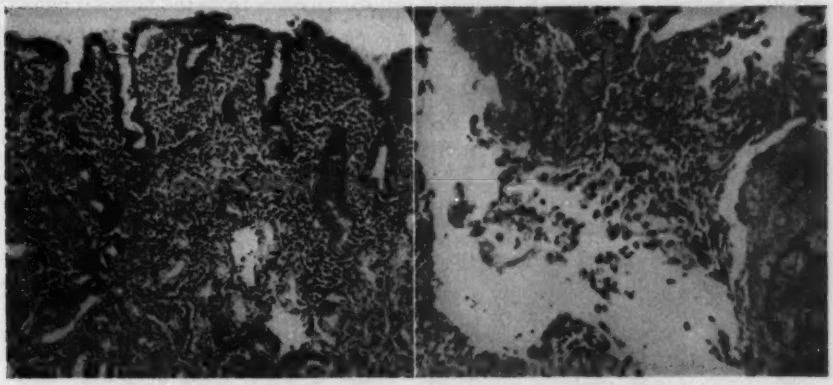

Fig. 6 Fig. 7

Fig. 6—Superficial erosive changes. Interstitial infiltration. Fairly normal gland structure at depth of slide.

Fig. 7—Carcinoma—Biopsy through degenerate carcinomatous area. Showing presence of some glands —amorphous material and individual cancer cells—(Biopsy and Papanicolaou positive).

center of the tumor and as expected were not particularly significant or diagnostic of the gastric polyp. It did serve a useful purpose in differentiating these gastric polyps from other lesions such as early polypoid carcinoma and from more rare situations such as leiomyosarcoma. The tissue, as you can see from the photomicrographs, shows merely some increase in the stroma but is not at all diagnostic. We believe that it has saved the patients an exploratory operation and that we are safe in resting our diagnostic opinion on that of a benign gastric polyp. This does not mean that they can be forgotten in the future. These lesions should all be

TABLE III

	Cases	Clinical Diagnosis	Roentgen Diagnosis	Gastroscopic & Microscopic
Normal	20	23	29	20
Gastritis	25	7	6	25
Gastric Ulcer	17	18	19	17
Malignancy	9	14	10	9
Gastric Polyp	2	2	2	2

watched with a great deal of care because one cannot undertake to predict when malignant degeneration may occur. We would suggest that the patients be examined by x-ray and the gastroscope at least once a year thereafter and that they be followed clinically very closely.

Carcinoma

All of the problems of diagnosis of the stomach are related indirectly to the attempt to rule out carcinoma. The obvious aim of any biopsy in any part of the body is to establish beyond reasonable doubt the presence of carcinoma. The difference between benign and malignant cellular changes from the mucosal biopsy is of the most significant importance as far as prognosis and treatment is concerned. As we have stated previously, a positive diagnosis of carcinoma or malignancy of other kind from a biopsy is an incontrovertible fact. This is a positive diagnosis which cannot be ignored in either the treatment or the prognosis. Again we would like to emphasize that a negative biopsy does not rule this localized disease situation out of the picture. A localized cancer can exist and not be biopsied. These patients who are suspected must be repeatedly examined by x-ray and by gastroscopic examination.

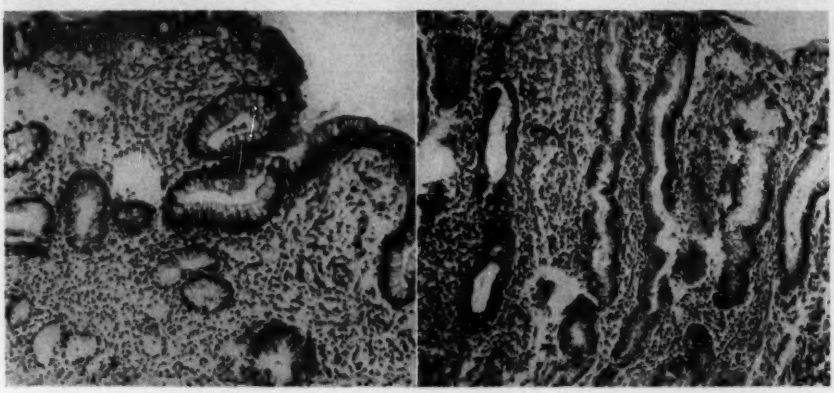

Fig. 8 Fig. 9

Fig. 8—Mucosal changes suggestive of Bowens-like metaplasia. Some interstitial atrophy plus some irritative glandular changes.

Fig. 9—Marked cellular changes probably on an irritative basis very suggestive of early malignant change.

In reviewing our experience with cancer of the stomach we believe that it is the most gratifying part of all of the cases that we have encountered. For instance the Borrmann Type IV submucosal infiltrating carcinoma is a much feared clinical entity. There are practically no reports in the literature of any cured cases of this kind. Schindler has made the statement that this is 100 per cent fatal. We have encountered two cases of submural or submucous infiltrating carcinoma Borrmann Type IV and Broder Grade IV. The x-rays were not diagnostic. Clinically in one case, the diagnosis was suspected and, in the other, the patient was felt to be a gastric neurotic. Biopsies showed very clearly this scirrhous type of carcinoma. Both patients were operated upon and one had peritoneal metastases which made resection impractical; the other had liver metastasis which made it unwise to undertake resection. In spite of these two occurrences it was gratifying to find

TABLE IV

DISTRIBUTION OF CASES

Case	Age	Sex	Final Diagnosis
1	59	M	Hypertrophic Gastritis
2	39	M	Gastric Ulcer
3	71	M	Carcinoma
4	26	M	Erosive Gastritis
5	54	F	Marginal Ulcer
6	65	M	Postoperative Stomach
7	47	M	Normal Stomach with Duodenal Ulcer
8	63	F	Gastric and Duodenal Ulcers
9	25	F	Postoperative Stomach
10	57	M	Normal Stomach
11	69	F	Gastric Ulcer
12	56	M	Postoperative Stomach
13	51	M	Hypertrophic Gastritis
14	72	M	Carcinoma
15	39	M	Normal Stomach with Duodenal Ulcer
16	45	M	Normal Stomach
17	26	F	Normal Stomach
18	66	M	Hypertrophic Gastritis
19	54	M	Gastric Polyp
20	30	M	Gastric and Duodenal Ulcers
21	74	F	Normal Stomach with Duodenal Ulcer
22	58	M	Carcinoma
23	40	M	Normal Stomach
24	55	M	Gastric Ulcer
25	40	M	Gastric Ulcer
26	48	M	Hypertrophic Gastritis
27	36	M	Carcinoma
28	47	F	Gastric and Duodenal Ulcers
29	34	M	Marginal Ulcer
30	51	M	Hypertrophic Gastritis
31	67	M	Gastric Ulcer
32	61	M	Atrophic Gastritis
33	48	F	Atrophic Gastritis
34	60	M	Carcinoma
35	64	M	Hypertrophic Gastritis
36	62	M	Hypertrophic Gastritis
37	59	F	Hypertrophic Gastritis
38	35	M	Hypertrophic Gastritis
39	54	M	Mixed Gastritis
40	49	F	Gastric Ulcer
41	54	M	Hypertrophic Gastritis
42	54	M	Normal Stomach
43	69	M	Atrophic Gastritis
44	35	M	Atrophic Gastritis
45	30	M	Postoperative Stomach
46	45	M	Gastric Ulcer
47	33	M	Erosive Gastritis
48	20	M	Gastric Diverticulum
49	71	M	Gastric Polyp
50	39	M	Gastric Ulcer
51	47	F	Gastric Ulcer
52	36	F	Normal Stomach
53	61	F	Gastric Ulcer
54	60	F	Normal Stomach
55	34	M	Hypertrophic Gastritis
56	40	M	Hypertrophic Gastritis
57	62	M	Hypertrophic Gastritis
58	58	M	Postoperative Stomach
59	59	M	Hypertrophic Gastritis
60	50	F	Normal Stomach
61	51	M	Normal Stomach with Duodenal Ulcer

TABLE IV (Continued)
DISTRIBUTION OF CASES

Case	Age	Sex	Final Diagnosis
62	60	M	Normal Stomach
63	52	M	Normal Stomach
64	57	M	Atrophic Gastritis
65	56	M	Postoperative Stomach
66	57	M	Normal Stomach
67	37	M	Normal Stomach
68	69	M	Carcinoma
69	68	M	Carcinoma
70	57	M	Normal Stomach
71	55	F	Carcinoma
72	44	F	Normal Stomach
73	54	M	Normal Stomach with Duodenal Ulcer
74	40	M	Normal Stomach
75	51	M	Polycythemia Vera
76	51	F	Gastric Ulcer
77	45	M	Normal Stomach
78	44	M	Tumor-Forming Hypertrophic Gastritis
79	58	F	Normal Stomach
80	55	F	Gastric Ulcer
81	63	M	Gastric and Duodenal Ulcers
82	56	M	Marginal Ulcer
83	33	F	Normal Stomach
84	37	F	Gastric Ulcer
85	31	F	Normal Stomach with Duodenal Ulcer
86	50	M	Postoperative Stomach
87	67	M	Hypertrophic Gastritis
88	36	M	Normal Stomach
89	57	M	Carcinoma
90	58	M	Hypertrophic Gastritis
91	19	M	Normal Stomach

that biopsies taken through the gastroscope were much more revealing than the biopsy specimens removed at operation. This is probably because this type of lesion infiltrates in the submucosa close to the mucosa and is spreading from there to the peritoneum. We are sure that if sufficient indication for gastroscopy is present that earlier cases of the scirrhous type carcinoma will be found by the gastroscopic biopsy. If this practical result follows then Type IV which makes up about 63 per cent of the cancers of the stomach will be amenable to early diagnosis and possible cure in the future. The other types, the polypoid mass of Borrmann Type I or II and the infiltrating wall of Type III can usually be well seen by x-ray. The gastroscopist who can see this lesion and remove a piece will have no doubt remaining in his mind, or in the mind of the other clinicians, that it is a carcinoma. We have used Borrmann as a gross classification for gastroscopic description and the Broder classification of grade for the degree of malignancy. We believe that from both a gastroscopic and surgical point of view these two classifications when used together will aid us in our evaluation and prognosis. The use of the random biopsy has been our attempt to eliminate the question of slowly growing infiltrating carcinoma with few symptoms that would not be found by other means. So far we have not encountered this particular early situation but we believe that it will be found eventually. The other forms of adenocarcinoma that we have encountered represent variously all of the Borrmann type of classification of tumor and some benign types of lesions.

Lymphosarcoma

This is a relatively rare situation which we have encountered only once. This is said with some trepidation because the case is not conclusive but was thought

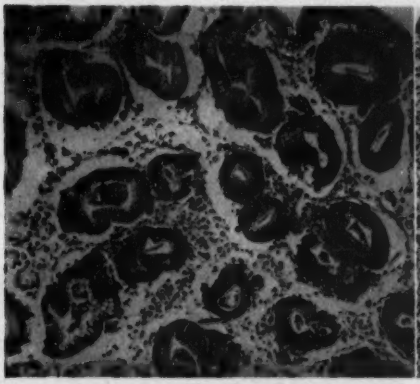

Fig. 10

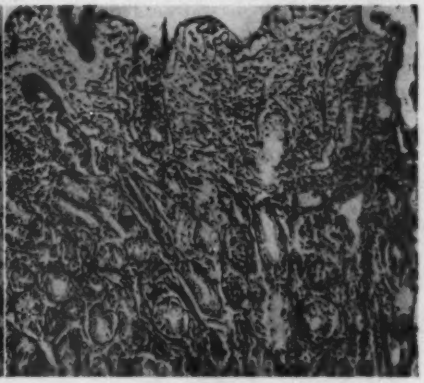

Fig. 11

Fig. 10—Gross specimen—Diffuse hypertrophic changes with gastric ulcer. Achlorhydric on 3 fractional analysis with caffeine and with histamine alcohol.

Fig. 11—Diffuse atrophic changes of both the surface epithelium—glands and interstitial tissue.

interesting enough to report in some detail. A forty-seven year old housewife entered the hospital with a good clinical story of gastric ulcer. This was well seen by x-ray and on gastroscopic examination. Biopsy of the ulcer edge and of the

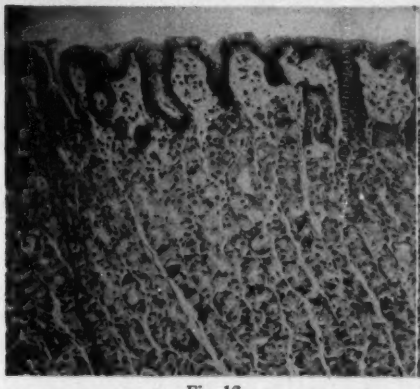

Fig. 12

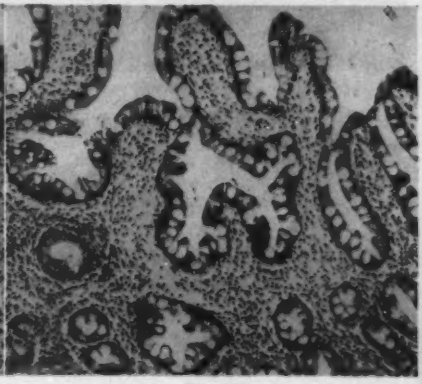

Fig. 13

Fig. 12—A good example of normal gastric epithelium showing gastric pits and normal distribution of typical gastric glands with a paucity of interstitial tissue.

Fig. 13—Polypoid hyperplasia of the gastric mucosa with a marked increase in number of goblet cells. The interstitial tissue in some areas gives a somewhat myxomatous appearance. Taken from a case which had cancer of the stomach. Shows definite changes in mucosa.

base showed some definitely abnormal cellular structure. This was not considered diagnostic of lymphosarcoma by the pathologist but was thought to represent

inflammatory infiltration. A routine chest x-ray examination showed a clearly outlined right lower lobe tumor. Exploration of the right lower lobe and a lobectomy revealed an encapsulated lymphosarcoma. These slides have been sent to various pathologists around the country and have aroused some discussion. First, the discussion has centered around whether it is benign or malignant. Most of the opinions have been that it is a malignant lymphosarcoma of the lung. Insofar as this is of about one year's duration and the patient was seen within the past week, is well and has had a perfectly normal healing of the gastric ulcer, has gained weight and feels fine, we are beginning to believe that it may be benign lymphoma in spite of the characteristics of the cellular structure of this tumor. Repeat gastroscopic examination six weeks after the lobectomy and another biopsy of the healed ulcer showed the inflammatory changes of healing. Therefore this may

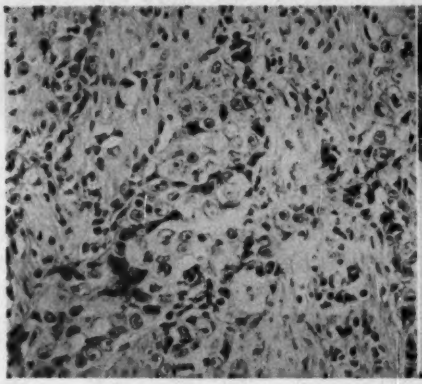

Fig. 14

Fig. 15

Fig. 14—High power—Carcinoma showing complete destruction of usual architecture. Many cells with mitotic figures—variations in size, shape and stain—quantities of malignant cells seen. May be actual extension into muscularis.

Fig. 15—Gross specimen—Section of base at one corner showing the area where the ulcer begins—typical mucrotic case. This is the ideal area for biopsy. Irritative changes in glands adjacent to ulcer.

well be a benign encapsulated lymphoma of the lung and the gastric ulcer a concurrent but independent disease process.

We have several other interesting cases that have been biopsied but the biopsy has not established the differential diagnosis because the findings in the stomach were only of a secondary degree process.

Polycythemia vera was encountered in a man of about 45 years who had, at the time of the gastroscopic examination, a blood count of about 10,000,000 red cells with about 24 gm. of hemoglobin. He was complaining of some of the typical gastric symptoms often associated with this disease. On inspection, the gastric mucosa was very red and appeared to be somewhat edematous and engorged. The tissue removed at biopsy was compatible with the primary diagnosis of polycythemia vera but it is not particularly diagnostic.

In addition to this, a patient with a gastric diverticulum was gastroscoped and biopsies taken. The biopsy showed no significant changes in the tissue. Many biopsy problems call for further investigation. The field of dermatology is replete with gastric associated lesions that should be biopsied.

Resume

The operating gastroscope has been used in 91 cases. The clinical findings and the microscopic findings have been studied in attempting to fit the overall pattern together. The normal stomach mucosa and the variation of gastritis cannot at this time be defined. There seems to be very little correlation between the gastroscopic diagnosis of gastritis and the microscopic findings.

Malignant and benign tumors can be differentiated and an accurate preoperative diagnosis be given if the lesion can be seen gastroscopically.

The procedure is safe and should be routinely used.

Conclusions

Routine biopsy should be a part of all gastroscopic examinations.

Tissue with objective evidence is added to the visual interpretation previously available.

Normal stomach tissue with variation cannot be defined at present.

Gastritis with its variable pattern cannot be classified and defined with our present experience.

Localized disease, that is, carcinoma *in situ,* localized gastritis, etc., is not excluded by a negative biopsy.

A positive biopsy, that is, one showing malignant tissue or cells is conclusive.

Discussion

Dr. Jean R. A. LeSage (Montreal, P. Q.):—After hearing Dr. Shallenberger's most excellent work and after reading the paper, there is a little bit of difference. When I read it, I felt rather protected from a clinical and gastroscopic point of view, but after hearing his added statistics and seeing his presentation of these wonderful microphotographs, I wonder if I shouldn't have come with the support of a pathologist. Anyway, I am consoled in hearing from Dr. Shallenberger that he is not a pathologist, so let's be more appeased.

The work of Dr. Shallenberger and his associates, Dr. DeWan, Dr. Weed, and Dr. Reganis, is undoubtedly, to date, one of the very few to offer such a well-documented exposé complete with statistics and microphotographs. This paper has a far-reaching message, if we consider the experience of the authors in the matter, and, after study, for an impartial analysis of the case, the results obtained.

It leaves the door open to enthusiasm in positive cases. It becomes very exacting in the negative ones, draws no conclusions, and asks for more facts, in such occurrences; however, early results allow us to forecast that the Benedict's type of operating gastroscope will eventually replace, in my opinion, the ordinary gastroscope, for this instrument holds triple advantages:

1. A good deal of better vision;
2. A proper aspirating process; and, chiefly,
3. A device for biopsy.

My opinion, based on those of a few authorities, and my own experience, dates back to studies with Dr. Moutier, in Paris, in 1931 and 1932; and a continual use of the gastroscope. In Montreal, a few thousand gastroscopies have been performed, since 1934, with the use of various types. Unfortunately, my experience with this operating gastroscope is very recent.

For the first two factors mentioned, the vision and the aspiration, especially with the smaller calibre in operation, only congratulations are in order. With regard to biopsy, although great hopes are well founded, on the other hand, a few possible uncertainties may occur.

As has been well emphasized by the authors, a well-chosen biopsy, of a positive nature, is unequalled by any other means, at that stage, and is final. A diagnosis is definitely reached; but, negative or normal after pathological study, the biopsy becomes valueless, and without significance.

This latter result may depend upon the inexperience of the operator, or, on the impossibility of access to the apparent visual site of a lesion, or, of a biopsy wrongly chosen through the operator's vision. Undoubtedly one must concede the tremendous personal factor entering in any form of endoscopy.

Thus, if this instrument is to be used accurately, it should not be considered primarily by the starting gastroscopist. May I here suggest that as numerous leading endoscopists have at some time or other encountered trouble, it would seem axiomatic that considerable experience should first be obtained with the simple gastroscope, before contemplation of the new operating gastroscope? Instead I suggest that this very instrument be handled by a junior endoscopist—perhaps we are all junior endoscopists—only after the use of a simple gastroscope, until, for example, hundreds of cases have been completed and what I might call until the "sense of visual objectivity" and "right interpretation" have been acquired. This is very arbitrary. That was an old condition of Dr. Schindler.

Which of the most common mistakes should be avoided?

1. A perforation of the gastric wall, mainly during an attempt at biopsy for a deep ulcer or, from an ulcerated cancer, when the biopsy is taken from the base or the bottom of the ulcer. Naturally, in case of doubt, it is better practice to take less, and perhaps, again, to repeat the procedure.

It is a fact that a more vivid illumination of the gastric mucosa, by a new power supply, such as has been in use in Canada for some time, may well facilitate a better vision of the site of a suspicious territory. Perhaps it will be possible to have sufficient light intensity to attempt to obtain photographs of those regions, with or without color, or, with or without motion, the resulting pictures of which will serve as basic documents to describe the aspects of a lesion which is positive, and to discard those which are negative. For teaching purposes the results would be invaluable.

My second point seems to be a most important one, and, as has been well mentioned by Dr. Shallenberger and his associates, namely, hemorrhages. We are assured by the authors that bleeding is but momentary. Actually, that is what all of us desire, but, when, after the contact of the tip of the simple gastroscope,

we often observe a bleeding or some erosions "which are causes of error", should we not be even more cautious lest we provoke a more severe bleeding when a biopsy is performed?

Why, then, should we not systematically have a gastric analysis with histamine test done, combined with a blood count, signature of a possible bleeding somewhere, then a prothrombin time and a proteinemia?

The patient would be properly prepared according to the conditions discovered, whether by transfusions, or Vitamins K and C, and so forth. May I also suggest that even if the results be normal, the blood viscosity and bleeding time be increased by a preparatory treatment of a few days of Vitamins K and C, and more protein intake, prior to the biopsy?

Here one objection could be raised: Would not such a preparation change the gastroscopic picture? Personally, I think not, and, after all, Dr. Shallenberger and others have suggested the biopsy of so-called atrophic gastritis, or of the mucosa in pronounced anemia, is still most precarious and sometimes practically impossible.

Passing to further consideration of the very delicate question of gastritis in gastroscopy, as to whether there is a necessity for a biopsy when the clinical picture suggests a gastroscopy, here I would submit that such biopsy be performed as a matter of routine. This, I think, is a logical conclusion to the remarks of Dr. Shallenberger and his associates. Thus, cases which show an apparent gastritis, when there is none, would be taken care of, along with those which do not give the appearance of a visual gastritis and show, by biopsy, a positive picture of gastritis.

The same applies to diffuse carcinomatosis. Again, with rarer cases of infiltrating lymphoma, as pointed out by Dr. Shallenberger, and Dr. Benedict elsewhere, this procedure might assist in the finding of an unexpected lesion of this type, and decide upon a gastrectomy. Also, in suspected lesions of the upper parts of the stomach, esophagoscopy and biopsy might reveal malignancies undiscovered by the Benedict apparatus. In Patterson's sixty-six cases of carcinoma of the stomach, the method accounts for some cases.

In conclusion, firstly, I agree with Dr. Shallenberger that biopsies of apparent vegetating ulcerated cancers are more easily obtained, with less possible post-biopsy effects, than with simple, apparent ulcers.

Secondly, I would suggest that for the benefit of all of us, a method of standardization be adopted which would include the whole pathological procedures, such as the preservation of material obtained by biopsy, the various stains required and used, and the minimum interval of time between the taking of the biopsy to the time when it is examined by the pathologist. This method would include the cytologic examination, perhaps by the use of Dr. Gladstone's gelfoam sponge pushed down the operating channel, and studied on both sides.

Perhaps we still remember some of our Euclidian problems, one of the most important of which was: "Things which do not equal the same thing, do not

equal one another". This great train of thought holds as true for the procedure of endoscopy as it does for that of pathology, and I am sure on that we will all agree.

Dr. Samuel Weiss (New York, N. Y.):—With reference to the method described by Dr. LeSage, we at the Polyclinic Hospital use gelfoam sponges wrapped around a stomach or duodenal tube and then the tube is passed into the stomach where it comes in contact with the affected area.

After the tube is withdrawn the sponge is fixed and sectioned like any other biopsy specimen and the sections are examined for cancer cells.

This gelfoam sponge method was originally introduced by Dr. Gladstone, pathologist at the hospital.

I want to make this correction.

Dr. Frank R. Fabiani (Dobbs Ferry, N. Y.):—Have you found cases where he has had a negative biopsy and positive Papanicolaou? Also, is it not true that ulcers on the greater curvature are practically always malignant, and do you biopsy those, too, or, rather consider them as malignant?

Dr. Paul L. Shallenberger (Sayre, Pa.):—In answer to the last question first we have had only one negative biopsy with malignancy found at operation. I was unfortunate enough to run across a case with two gastric ulcers, both on the lesser curvature. One ulcer on biopsy, was entirely benign, and neither the x-ray nor I saw the other ulcer. It was apparently buried in edema or edematous scar tissue and was malignant when it was removed surgically. There was enough indication in this case because of previous failure to heal to do a subtotal gastric resection. The lesion was restricted to the ulcer.

I think all gastroscopic examinations should include biopsy. The fallacy of biopsy of a gastric ulcer really is twofold. A few of them in the prepyloric region cannot be seen gastroscopically. Dr. Berry's methods of moving the patient to the right side or on his back, or the method of sitting them up in a chair, will help a great deal in localizing lesions that cannot be seen otherwise. It is necessary at times to undertake a great deal of ingenious movement and palpation pressure of the abdomen of the patient.

The second fallacy is one that may be corrected with further experience. It is most difficult to direct the biopsy forceps to the exact location in an ulcer that you see. Aim and correlation of the instrument and forceps at such a distance from the objective are difficult mechanical feats.

It is generally accepted that an ulcer on the greater curvature of the stomach probably is a malignant ulcer. I would not regard a negative biopsy in an ulcer of the greater curvature as positive proof of its benign nature.

We have tried the gelfoam and several other methods for obtaining Papanicolaou material. Our experience would indicate that the amount of secretion that we can get by introducing a small aspirating, plastic tube into the area where we have taken the biopsy, or into the lesion, gives us a great deal more material. We can make multiple Papanicolaou stains on the material at once.

Dr. LeSage proposed several questions. I greatly appreciate his discussion. He made the statement that a negative biopsy may be valueless, or is valueless. I should like to point out that we have seen changes in the gastric mucosa at a distance from the lesion in carcinoma cases, and in gastric ulcer cases. I have the impression that eventually we are going to recognize these changes in the gastric mucosa and understand their importance. If that is true, then a negative biopsy may have more value in the future than it does at present.

Dr. LeSage put the number of fifty to one hundred examinations as the experience necessary for background in gastroscopy. I would say that is a conservative estimate. I think you will have to see at least five hundred stomachs before you know what the inside of one looks like.

The ideal, eventually, should be to have a gastroscopic examination with a good look at the entire inside of the stomach; the ability to take a picture with the same gastroscope in place, of any pathological lesion that is seen; and the ability, again without removing the gastroscope, to take a bite of the pathological lesion seen.

We have not encountered any massive bleeding. I have taken about fifty of these cases and run daily chemical tests for blood in the stool. If they have been on a meat-free diet, I have yet to find a case with a positive test. Stools have been followed for about a week in each of these cases.

We have not used topical thrombin but have had it available. The stomach has stopped bleeding, in every case, in about twenty seconds or less. It is amazing to watch the rapidity with which the tissue contracts and stops bleeding while you are looking at it.

We have also tried to powder oxycel gauze, and have found it difficult to get down the small tube where the biopsy forceps go.

In atrophy we intentionally stayed away from the blood vessel because we were afraid of bleeding, and took the bite of tissue in the silver blue area adjacent to the blood vessel.

In lesions of the cardia, where the x-ray shows any evidence of obstruction at the inlet of the stomach, the patient is always subjected to esophagoscopy first, and the entrance of the stomach is evaluated from the esophagoscopic view, and biopsies are taken. In three or four of these cases the lesion had encroached on the esophagus, but we have been able to get through without difficulty, and the biopsy of the cardia by the gastroscope, has been better than the view of the lesion and the biopsy through the esophagoscope.

CLINICAL X-RAY CONFERENCE ON LOCALIZED CONSTRICTING LESIONS OF THE COLON*

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X-ray demonstration of a localized constricting lesion of the colon presents a fairly common problem of differential diagnosis. No attempt will be made here to discuss the subject comprehensively but rather to illustrate some of the possibilities and some of the problems which may arise.

Case 1:—L. H., woman, age 49. The presenting symptom was bleeding from the rectum of 18 months' duration with persistent cramping in the abdomen. She

Fig. 1—Case 1. A short area of constriction is present in the lower sigmoid colon. Its transition to normal colon is abrupt. Overhanging edges of the barium column are seen at its distal end. The channel surface is irregular. The entire appearance is typical of malignant neoplasm primary in the colon and forming an annular growth.

had had four abdominal operations, performed elsewhere, the first a left salpingectomy and oöphorectomy, the third a hysterectomy, the other two for division of adhesions because of episodes of bowel obstruction. At the last operation, six years before the present illness began, multiple implants on the small bowel, kidneys, ureters, bladder and colon were found and proved to be endometrial tissue. However, the remaining ovary was not removed nor was x-ray sterilization per-

*Read before the Fifteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 9, 10, 11 October 1950.

formed. The patient had not noticed any relation between bleeding from the bowel and menstruation but the abdominal cramps were worse during the menstrual periods.

Fig. 1 demonstrates the lesion found by barium enema. The history certainly suggested that endometriosis of the colon or deformities due to peritoneal scar tissue will be found but the constriction present was localized, fairly short area in the mid-sigmoid. Its margins were abrupt and showed overhanging edges. The channel through the lesion presented an irregular surface. The x-ray appearance was typical of malignant neoplasm arising in the colon and growing in annular fashion.

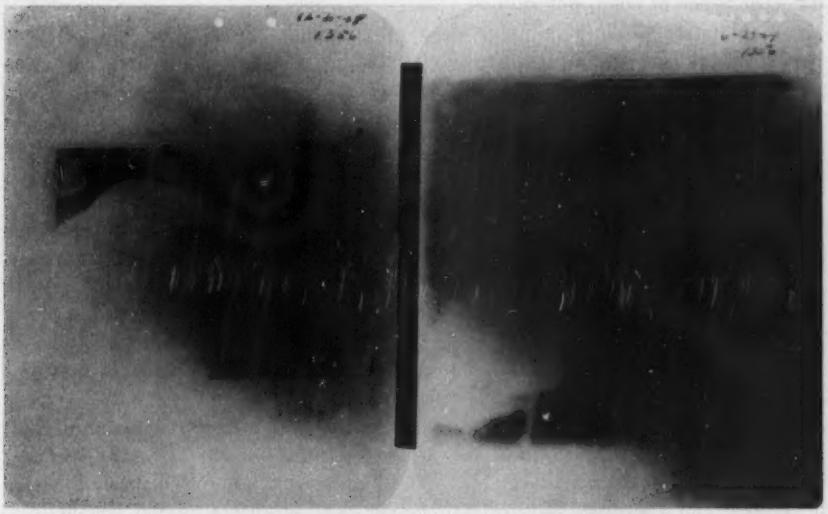

Fig. 2—Case 1. The right hand film shows the long, tapering narrowing of the colon produced by the extrinsic pressure of a large mass. The channel is fairly smooth. A film of the earlier primary malignant neoplasm is included on the left for comparison.

Laparotomy demonstrated numerous small, hard, shot-like implants studding the peritoneal surfaces, apparently the residue of the previous endometriosis. Several loops of small bowel were adherent to a mass in the sigmoid colon. These loops were resected and anastomoses done. The sigmoid was resected and anastomosed.

Microscopic examination of the surgical specimen revealed adenocarcinoma of the colon, grade II, with local extension, also chronic peritonitis with demonstrable talc granules present.

The patient remained well for five months and then experienced a feeling of fullness in the pelvis and symptoms of moderate obstruction. She returned one year after the removal of the sigmoid carcinoma. A grapefruit-sized pelvic mass was palpable.

Barium enema was again administered (Fig. 2). Again there was a narrowing of the colon above the rectum. This time, however, the deformity was long and its ends were tapering rather than abrupt. An exposure of the earlier lesion in the same angle of projection is included in the figure on the left for comparison. The history now suggested recurrence of carcinoma of the colon but the smooth and regular channel through the lesion indicated that the narrowing was due to extrinsic pressure. Fig. 3 shows that a very large oval soft tissue mass filled the right side of the pelvis. The findings were a typical example of deformity produced by extrinsic pressure by a mass which did not involve the colon. This case is presented to demonstrate the contrast between the x-ray appearance of these two different types of colon deformities.

Exploration disclosed a large right ovarian mass fixed to all the adjacent pelvic viscera and to the iliac vessels. Resection was done and ileostomy was performed.

The surgical specimen consisted of a ragged mass 10 by 5 cm. which on dissection proved to be an enlarged ovary together with its attached oviduct; the ovary was 5 cm. in diameter and on cross-section showed a solid cellular tumor growth which replaced all of the ovarian parenchyma. The tube was irregularly dilated and both organs were covered by thick adhesions. Microscopically the ovarian tumor represented an adenocarcinoma of indeterminate origin although it appeared to be metastatic rather than primary in the ovary. The lymphatics of both tube and ovary contained numerous tumor cells, indicating extension along these channels.

The patient's condition showed progressive deterioration and death occurred six months later.

Case 2:—J. Z., woman, age 43. The patient presented a complaint of dull aching pain in the left lower quadrant of seven months' duration, becoming cramping and colicky during the two weeks before admission. There had been episodes of nausea, and vomiting, signs of obstruction, and a thirteen pound weight loss. There was no history of menstrual disturbance. Proctoscopy was negative.

Films demonstrated an area of constriction in the distal sigmoid colon (Fig. 4). The area of involvement was unusually long for neoplasm. While the ends of the lesion were abrupt, they do not present the typical overhang found in most malignancies in this portion of the colon. Obviously, the radiologist could not definitely exclude the possibility of a primary malignancy, but on the basis of this evidence suggested that an inflammatory etiology was more likely.

A transverse colostomy was done first. Exploration at that time revealed very dense adhesions and a large mass in the pelvis. Endometriosis or diverticulitis with inflammatory mass was suspected, but malignancy still could not be ruled out. In a subsequent operation, the mass was resected with its segment of sigmoid colon. The remaining colon was anastomosed, and total hysterectomy and bilateral salpingo-oöphorectomy were done. The transverse colostomy was later closed.

The resected sigmoid segment showed a napkin-ring type of annular thickening extending two-thirds of the distance around its circumference, the center of

the lesion being in the mesocolic attachment. Cross-section through the lesion showed a tumor infiltrating the muscle wall of the colon up to the submucosa, with the mucous membrane still freely movable over the lesion, and apparently intact. The uterus exhibited mural thickening and several typical fibroid tumors, while the adnexa were boggy and their serosal coverings thickened and opaque, with many adhesions. Each ovary contained several chocolate cysts. Microscopically the colonic lesion was a typical growth of aberrant endometrial glands and cytogenic stroma, associated with some benign desmoplasia. The uterus, tubes and ovaries were involved in a remarkably extensive infiltration by similar endometrial tissue showing more or less secretory activity, with some bleeding into the lumina.

Fig. 3—Case 1. The very large soft tissue mass seen in the right pelvis produces the deformity of Fig. 2 by pressure on the colon.

The diagnosis of endometriosis of the colon is usually made by combining x-ray findings of a constricting lesion not typical of carcinoma (as in this case) with history of intermittent symptoms at their worst just before or during the menstrual periods. In this case the periodicity of symptoms was completely absent and the menstrual history normal, preventing establishment of the correct diagnosis preoperatively.

Case 3:—T. S., woman, age 40. The patient was a very malnourished woman, weighing 85 pounds, complaining of left upper quadrant pain and diarrhea of fifteen years' duration.

Fluoroscopy and films demonstrated an irregular, 6 cm.-long area of constriction in the proximal descending colon (Fig. 5). As in the last case, the transition to normal-appearing colon at the ends of the lesion was fairly abrupt but without the typical overhang of the napkin-ring primary colonic malignant tumor. The channel through the lesion showed a coarser pattern of irregularity than is common in carcinoma of the colon, suggesting broad flat ridges of tissue. The radiologist concluded that the lesion was "probably a granuloma, a carcinoma or a lymphosarcoma".

Operation consisted of segmental resection of the stenosed area of the splenic flexure with primary anastomosis. A loop of small bowel caught in the mass was also resected, and primary anastomosis was done.

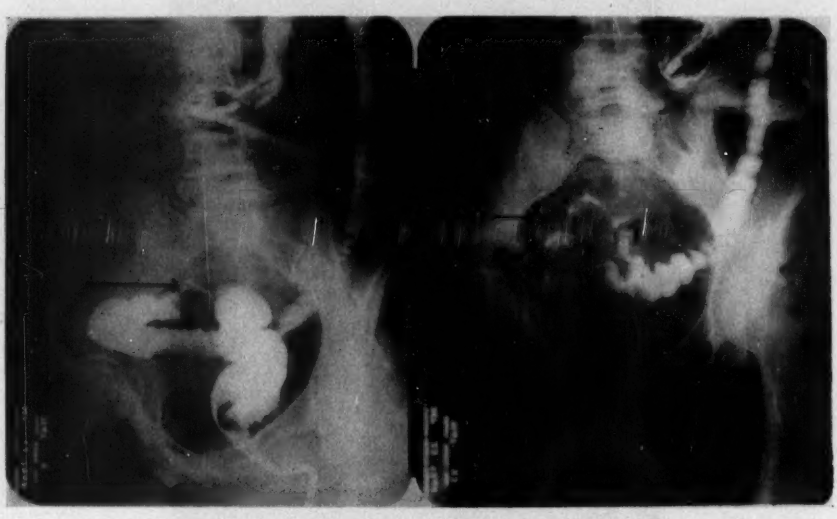

Fig. 4—Case 2. The constriction in this case is rather long. Its channel is irregular as in annular carcinoma but not as well centered at its junction with normal colon as is expected. The margins are abrupt but there is no overhang of the barium column at the distal end of the lesion. This constriction is therefore not typical of carcinoma of the colon and was not carcinoma.

The surgical specimen was a portion of colon 20 cm. long, showing marked thickening of its middle third, at which point it was firmly adhered to a loop of small bowel. Cross-section through the two adherent loops revealed a mass of indurated omental fat and a single small central abscess pocket containing pus; the latter was located opposite the blind tip of a diverticulum about 1 cm. deep which projected into the mesocolon from the gut lumen, and which showed congestion and apparent necrosis of its distal wall although no actual perforation could be demonstrated. Numerous other similar diverticula were scattered along the entire length of the specimen, most of these being located at the site of its mesocolic attachment. No tumor could be demonstrated, either grossly or microscopically;

microsection revealed subacute and chronic nonspecific inflammation with one small abscess containing mixed bacteria.

A preliminary cecostomy had been done to insure the integrity of the anastomosis. After several unsuccessful attempts at closing the cecostomy during the first postoperative year, it was thought advisable to improve the patient's nutrition. She was instructed to gain twenty pounds of weight before closure was again attempted.

Radiologic check-up one year after the initial surgery was made difficult by the presence of a fistula between small bowel and colon at the site of the previous resection. Rapid escape of barium into the small bowel prevented good distention

Fig. 5—Case 3. This constriction is fairly long. Its ends are tapering. The channel shows broad, flat areas of irregularity rather than the fine irregularity usually seen in carcinoma. Granuloma or lymphosarcoma must also be considered.

of the colon. However, it was apparent that a fairly long area of marked narrowing was present in the left transverse colon (Fig. 6).

At the operating table conditions identical with those originally encountered were found. About 5 inches proximal to the colonic anastomosis and about 5 inches proximal to the jejunal anastomosis, we found a jejunocolic fistula. Segments were removed and an anastomosis was done in each instance. The cecum was then mobilized and closed and the patient has remained quite well since.

Microscopic examination revealed only chronic granulomatous inflammation of nonspecific character.

This was an unusual case of chronic, nonspecific granuloma of extremely long duration, presumably secondary to infection of diverticula extending into the mesocolon.

Case 4:—E. L., woman, age 53. This patient had a history of ruptured diverticulitis of the sigmoid one year previously. She told us this had been surgically drained and a transverse colostomy performed, and later closed when the mass subsided. A month later a cholecystectomy had been performed and it was reported that exploration at that time showed diminution of the mass. Six months later a left lower quadrant abscess had been drained. On admission, she presented an irregular, firmly fixed mass in the left lower quadrant, the size of a small grapefruit. There was rectal bleeding. The patient's general condition was surprisingly good, and there was no net weight loss.

The first two films (Fig. 7)*, were taken four months apart. A small filling defect is present at the junction of the descending and sigmoid portions of the colon in the first examination. It is not annular, and it presents two pointed lateral extensions of barium, suggesting the necks of diverticula. This film certainly sug-

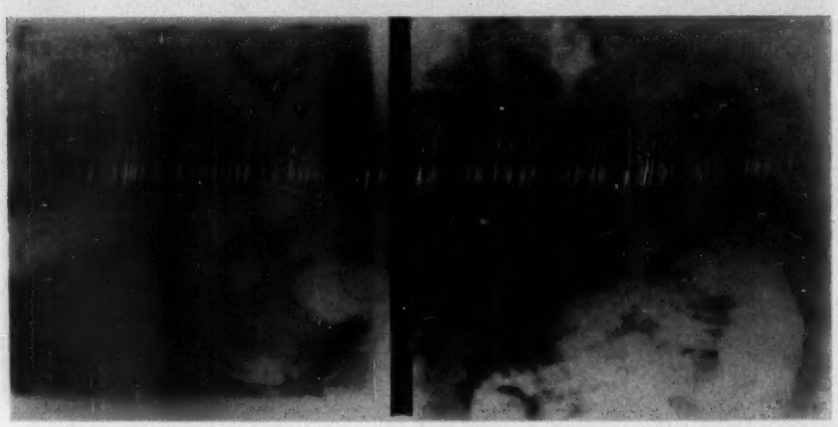

Fig. 6—Case 3. These spot films of the left transverse colon demonstrate a long, tapering constriction. The small bowel filling was due to fistula at this point.

gests a diverticulitis. The second film showed that an annular filling defect was present resembling malignant neoplasm.

Six months later here (Fig. 8), the colon was seen to circle around the medial and posterior aspect of a 12 cm., hard, left lower quadrant mass. There was much deformity of the colon, largely produced by extrinsic pressure of the mass. Long before the entire colon was filled, barium appeared in several loops of small bowel, indicating a fistula between the large and small bowel. Since this phenomenon appeared at the time the barium reached the area of previous colostomy in the mid-transverse, it was erroneously assumed that the fistula was at this point. The long history and the large pericolonic mass with irregular, nonsymmetrical deformity of the colon, together with the diverticulous points extending from the

*Courtesy of Drs. Holly and Joistad, Muskegon, Michigan.

colon in the earliest film, led us to a diagnosis of diverticulitis with a large pericolonic inflammatory mass.

Transverse colostomy was done and the mass explored. It was thought that it might be a diverticulitis; however, because of the density of the adhesions, the question of endometriosis was entertained. Two frozen sections failed to demonstrate neoplasm but, as the dissection progressed, it gradually became apparent that a malignancy was present. A large mass involving the sigmoid was resected. It was necessary to fractionally resect and anastomose the small bowel five times and, of course, anastomose the large bowel deep in the pelvis. The patient had an uneventful recovery after an eight hour surgical procedure.

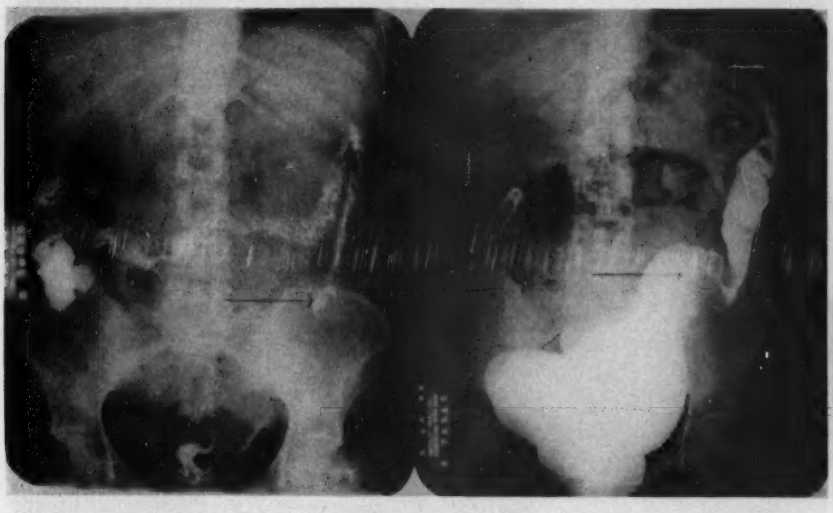

Fig. 7—Case 4. The left hand film illustrates the original examination of this patient. The deformity suggests the presence of diverticula with active inflammatory process. The right hand film, four months later presents the appearance of an annular primary carcinoma of the colon.

The transverse colon still remained to be anastomosed and dropped into the abdomen. After a year's delay, she was again admitted for study and surgery. Barium enema (Fig. 9) again showed a gross filling defect of the descending colon. This time it was somewhat above the area of previous resection. It was a large intraluminal mass with a broad base on the lateral wall of the colon and indicated recurrence of neoplasm. This intraluminal growth presented a much more typical appearance than the original growth which was largely outside of the colon.

At the operating table, it was found that the descending colon contained a very large neoplasm which almost entirely encircled the kidney on that side. There was considerable seeding and miliary spread throughout the lower pelvis and left abdomen. Obviously, a cure was impossible, therefore, the abdomen was

closed and the patient was left with a transverse colostomy. She died a few months later.

This case was unusual and misleading because of the slow development of the neoplasm, the amazing continuance of good general condition long after widespread carcinoma was present, and the largely extracolonic nature of the growth. It is distinctly uncommon to find very large abdominal masses due to local extension of carcinoma of the colon in patients in excellent general health. In retrospect the presence of the fistulae offered a definite hint of the underlying neoplastic nature of the mass.

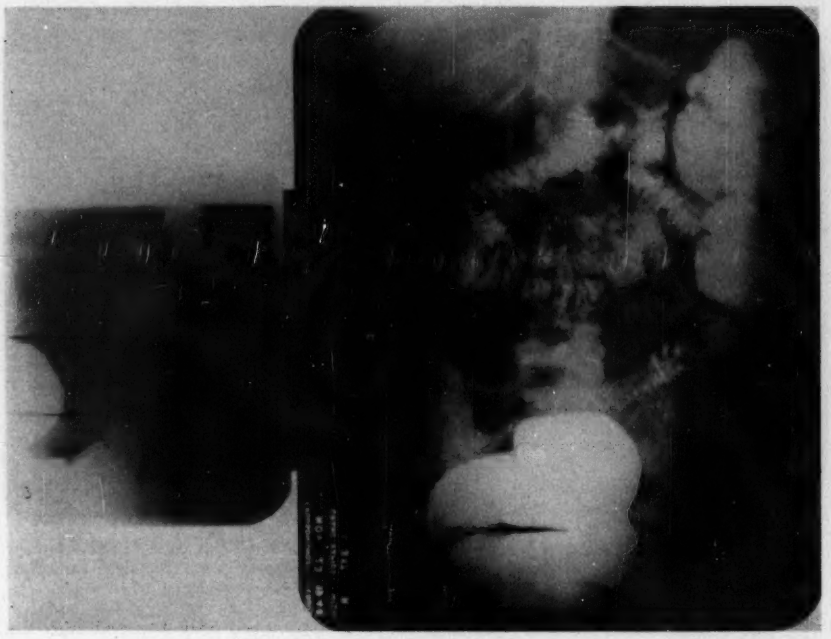

Fig. 8—Case 4. The third examination of this patient, one year after the first, shows a very deformed segment of colon circling about a very large extracolic mass.

Case 5:—A. S., woman, age 44. This patient was first seen for a small anorectal fistula and bleeding hemorrhoids. Her mother, age 75, at that time was treated at the clinic for an adenoma simplex of the rectum. Because of the mother's findings, the daughter was referred for barium study of the colon.

Fluoroscopy demonstrated two diverticula of the sigmoid colon with slight irregularity and narrowing of the colon at this point as shown also by the films (Fig. 10). Deformity of the sigmoid colon due to spasm and/or inflammatory thickening of the wall or due to pericolonic inflammation is, of course, common in

diverticulitis. The diagnosis of deformity due to diverticulitis was made but the radiologist hedged by requesting follow-up examination for further study of the area.

Fortunately sigmoidoscopic examination revealed evidence of a movable tumor, probably based in the mid-sigmoid. Biopsy showed grade II, adenocarcinoma. At the operating table, the sigmoid appeared to be in fairly good condition. There was minimal diverticulosis and the two polypi could be easily palpated. A segmental resection was done with end-to-end anastomosis.

The specimen was a portion of colon 35 cm. long submitted with its mesenteric triangle still attached. Two sessile polypi 24 mm. and 12 mm. in diameter respectively were growing from the mucosa of the resected segment; their covering

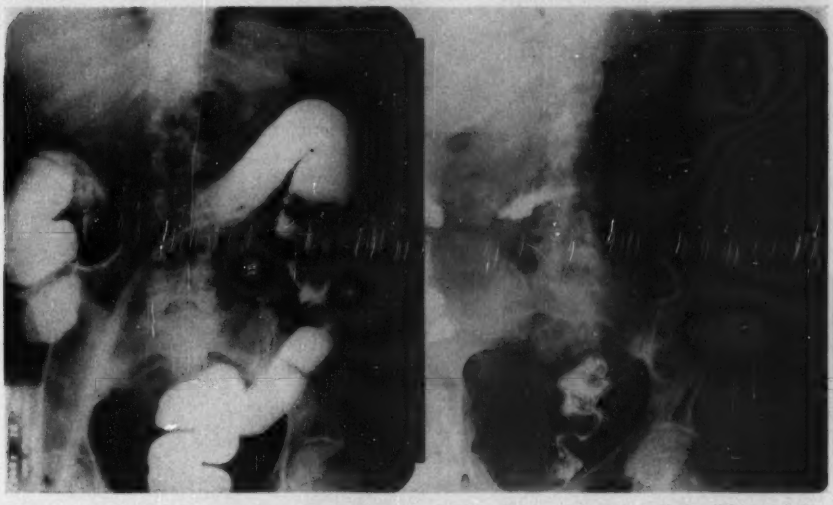

Fig. 9—Case 4. The deformity found a year later (one year after resection) is entirely different, being an intraluminal mass just above the area of anastomosis.

epithelium was quite obviously hyperplastic and on cross-section the pedicles of both tumors were filled with neoplastic tissue which was commencing to invade the subjacent colon. Microscopically the two tumors were malignant polypi of somewhat different cytology and obviously of separate origin; both had commenced to involve the lymphatics of the muscle wall directly beneath their pedicles, but without evidence of extension beyond the limits of the colon proper.

Review of the roentgenograms in the light of these findings indicates that the deformity seen was undoubtedly due to the small malignant polypi. In this case the pathologic specimen did not show evidence of inflammatory change, so the x-ray diagnosis of diverticulitis was incorrect.

The situation in which deformity due to diverticulitis may coexist with neoplasm in the same area is a somewhat similar source of diagnostic error. Since

neither diverticulitis nor neoplasm of the sigmoid colon is uncommon it is inevitable that they will exist concurrently in some few patients. It is quite likely that in that circumstance, the deformity produced by a small neoplasm will be obscured by a more extensive deformity due to diverticulitis. Certainly the danger must be recognized and evaluated in every case of diverticulitis.

Three procedures are available to avoid long delay in recognition of a growth in the presence of diverticulitis. One is very thorough sigmoidoscopy with biopsy of any suspected area. That saved the day in the somewhat parallel situation of the present case. A second is reexamination by barium enema and by sigmoidoscopy after the diverticulitis has received two or three weeks of medical management.

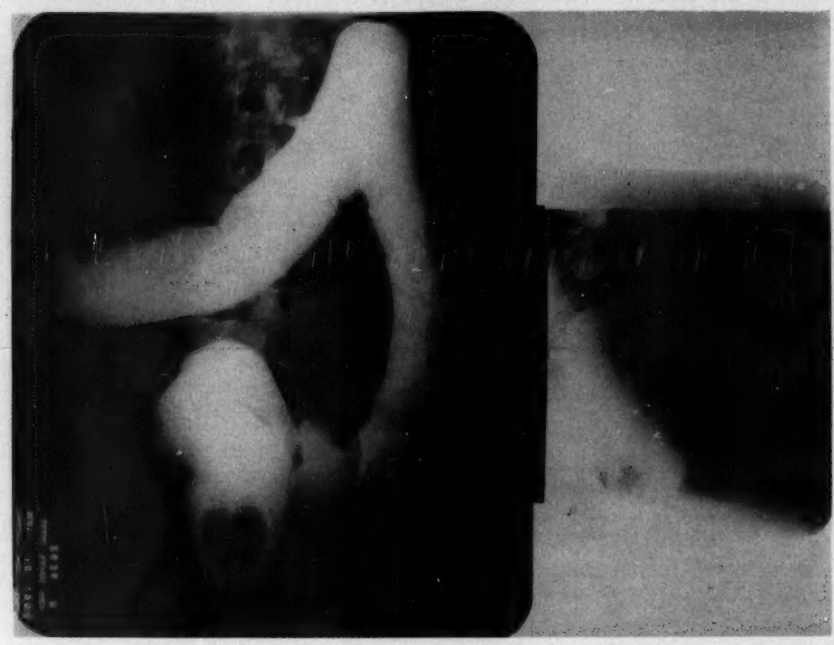

Fig. 10—Case 5. Two small diverticula are present rising superiorly from the mid-sigmoid colon. There is deformity of the lumen localized to this area raising the question of inflammatory process secondary to the diverticula or concurrent neoplasm.

Since the deformity of diverticulitis is very variable, depending on the severity of the inflammation present at the moment, re-ray will often demonstrate a good, even lumen enabling one to rule out the possibility of hidden neoplasm. Lastly it seems evident that in occasional cases laparotomy and resection of the area of diverticulitis should be done if there are any clinical grounds to suspect that it may be hiding a small area of neoplasm.

Case 6:—D. G., man, age 74. The symptoms were abdominal distention, difficulty in passing gas, frequent passage of mucus and 15 pound weight loss. They were of two years' duration.

Digital examination revealed a small mass in the proximal rectum.

Roentgenologic findings are illustrated in Fig. 11. A broad-based, rounded mass was present in the rectum—a polypoid tumor which might be either malignant or benign (malignant in this case). There was also a short annular constriction of the distal sigmoid, with abrupt overhanging edges and a tortuous channel. This was a typical annular malignant neoplasm. In this case neoplasms were demonstrated at two separate locations.

A one-stage combined resection was done with a generous mobilization of descending colon to remove as many as possible of the regional nodes. The patient

Fig. 11—Case 6. A large, round polypoid type of growth is present in the left side of the rectum. The annular constriction of the distal sigmoid is another neoplasm of totally different growth characteristics.

has regained his weight and made a satisfactory adjustment. The prognosis is, of course, guarded.

The pathologic specimen was a portion of terminal colon including the anal sphincter 40 cm. long showing a cauliflower adenocarcinoma 4 cm. in diameter which involved about one-half the gut circumference. At the rectosigmoidal junction a second somewhat different looking carcinoma 3 cm. long was present, and between the two tumors were several small benign polypi. Microscopically both lesions were definitely malignant and had invaded part way through the gut wall

without demonstrable enlargement of the regional lymphatics. The two were distinctly different histologically and represent separate primaries.

Double primaries of the colon are uncommon but not rarities. Every clinic has one or more in its files. We have seen two during the past three years. They will be missed unless every patient—no matter how obvious the initial rectal findings may be—is thoroughly checked by sigmoidoscopy and barium enema.

Case 7:—W. D., man, age 49. The patient had noted right lower quadrant discomfort for two weeks. It was relieved from time to time by passage of loose stool. There was no history of bleeding or secondary anemia but the patient tired easily and had lost appetite. Slight weight loss had occurred. Appendectomy had been done at age 14.

Fluoroscopy demonstrated an irregular filling defect of the cecum. This is demonstrated (Fig. 12) in films made with barium filling, after evacuation, and after air filling. The terminal ileum could not be filled. The x-ray report noted

Fig. 12—Case 7. A filling defect of the cecum is demonstrated in preevacuation, postevacuation and double contrast films. In the postevacuation film it appears annular.

that: "The most likely etiology is a malignant neoplasm. However, an infectious granuloma might produce the same appearance", and concluded: "Mass within the cecum based on the medial wall and tip of the cecum, presumably a malignant neoplasm".

Decompression was carried out and then exploration. The liver was negative to palpation and there was no evidence of epicolic, paracolic or aortic nodes. There were dense adhesions throughout the pelvis and particularly in the right lower quadrant and around the cecum. A large, hard mass involved the cecum and terminal ileum. Its gross appearance and consistency suggested malignancy. The right colon and distal ileum were resected and ileotransverse colostomy was accomplished without incident. It was noted that the terminal ileum was coiled on itself and adherent to the cecum in the region of the former appendectomy procedure.

Pathological Report:—"The surgical specimen includes a portion of terminal ileum 75 cm. long and the proximal half of the right colon 35 cm. long. Thick

adhesions are present in the ileocecal angle especially on the posterior aspect of the gut where the serosa is frayed and markedly thickened and congested with a small pocket at one point resembling an ancient abscess cavity which is now dry; a stump of appendix 2 cm. long is buried in the adhesions at this point. The terminal 15 cm. of ileum is diffusely and symmetrically thickened with some sessile polypoid hyperplasia of the mucosa but no ulceration of the latter; these polypoid masses evidently represent hyperplastic lymphoid tissue. The thickening ceases abruptly at the ileocecal valve and the colon itself appears normal. Numerous rubbery lymph nodes are scattered through the triangle of mesentery still attached to the specimen.

Fig. 13—Case 8. The rectum is constricted to fairly uniform diameter throughout its length. The mucosal surface is highly irregular.

"Microscopically the essential lesion is a nonspecific hyperplasia of lymphoid tissue in the mucosa of the terminal ileum with superficial ulceration at some points; this is associated with extreme edema and fibrosis of the submucosa, hypertrophy of the muscle coats, and an exuberant chronic granulomatous reaction in the serosa and mesentery, the latter including numerous foreign body giant cells and a dense leucocytic infiltration which includes many eosinophiles. Polarized light reveals large numbers of refractile crystals scattered throughout the inflamed area and a smaller amount of similar material in the regional lymph nodes described above. There is no suggestion of carcinoma, tuberculosis or specific lymphogenous tumor.

"*Conclusions:*—Chronic peritonitis of foreign body type probably talc with secondary terminal ileitis due to lymphatic stasis."

Case 8:—M. H., woman, age 48, colored. The patient was referred to this clinic because of multiple fistulae of two years' duration at the anal outlet. She had shown moderate signs of obstruction. Examination revealed a very stenosed anal outlet which was hard and unyielding. The Frei test was positive.

The x-ray examination was performed with difficulty because of inability of the stiffened, tube-like rectum to retain an enema tube. The entire rectum was seen to be markedly constricted and rigid, with marked irregularity of its surface. Barium leaked from the vagina during examination, through a rectovaginal fistula which was apparently very near the introitus since films (Fig. 13) did not show any retention of barium within the vagina. The proximal colon was negative.

These findings are typical of lymphopathia venereum.

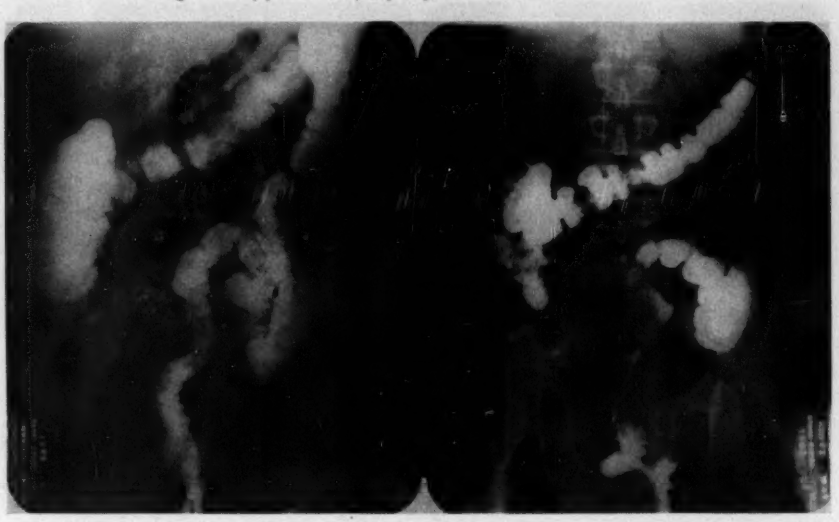

Fig. 14—A similar case. Note also the presence of sinus tracts in this example.

(Fig. 14 demonstrates a similar case. Note the extreme length of involvement, the marked irregularity of surface, and the rather even degree of constriction. Sinus tracts are present. The rounded mass near the anus is a superimposed malignancy.)

A one-stage combined resection of the rectum was done leaving a single barreled colostomy. Convalescence was uneventful with excellent healing and recovery.

The specimen was a portion of terminal colon 22 cm. long including the anus and adjacent skin. Ten cm. above the sphincter there was a rather high grade stenosis of the gut due to an irregular thick-walled ulcerating lesion 7 cm. long involving its entire circumference and characterized by marked irregular scarring of the entire thickness of the rectal wall as well as of the attached mesocolic fat with some degree of involvement of the entire terminal segment down to the anal orifice. Microscopic examination revealed an unusually severe atypical chronic

granulomatous inflammation involving almost the entire length of the rectum and characterized by marked fecal proliferation of lymphoid tissue and a diffuse infiltration by all types of leucocytes including many plasma cells and eosinophiles, together with dense scarring and the formation of numerous sinus tracts in and about the rectal wall.

Case 9:—B. F., woman, age 51. The patient was referred because of alternating constipation and diarrhea with occasional rectal bleeding during the previous three months. There had been short episodes of colicky pain relieved by diarrhea. The patient stated that a radium treatment of thirty-six hours duration had been

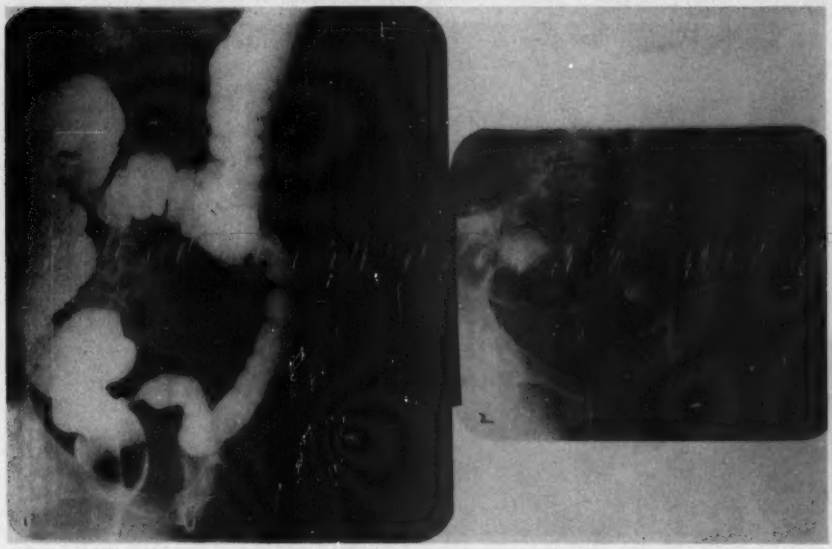

Fig. 15—Case 9. There is a short, symmetrical constriction of the sigmoid colon. Its margins are abrupt. It should certainly bring to mind the (erroneous) diagnosis of primary malignancy of the colon.

done five months previously for abnormality of the cervix. The amount of radium used is not known.

Digital examination did not reveal any significant abnormality. Sigmoidoscopy could not be satisfactorily performed because of fixation of the sigmoid colon deep in the pelvis producing a sharp angulation of the colon through which the instrument could not be passed.

We believe that the radiologist should have full knowledge of what the clinical situation is before investigating it, to be certain that the investigation will be such as will reveal as fully as possible the positive and negative findings which may be pertinent to that particular situation. Therefore he obtained the history of radium treatment before beginning fluoroscopy and had in mind the possibility of radiation

fibrosis of the colon or of secondary involvement of the colon by neoplasm arising in the uterus. However, the lesion found at fluoroscopy and illustrated by Fig. 15 presents the typical appearance of primary carcinoma of the colon. The lesion is short, symmetrical and abruptly terminated, in contrast to the diffuse smooth tapering and surface irregularity usually found in radiation fibrosis or the long asymmetrical deformities produced by invasion of the colon by neoplasm of pelvic origin. The only missing text-book feature of primary colon neoplasm is the fine irregularity of the surface of the channel present in that lesion.

The radiologist's conclusions were: "Short, markedly constricting lesion of the sigmoid colon, probably a primary malignant neoplasm of the colon".

Fig. 16—Case 10. The rectum fills the pelvis and lower abdomen extends to the 12th dorsal level. The sigmoid is also grossly distended. The proximal colon is enlarged but only slightly.

Laparotomy revealed a 5 cm. mass composed of a sharp angulation of the bowel adherent to the posterior aspect of the cervix in the pouch of Douglas. Anterior resection of the mid-sigmoid was done and primary anastomosis performed.

The pathological specimen was a portion of colon 14 cm. long, at the midpoint of which there was an annular ulcer 5 mm. wide completely encircling the gut; the ulcer margins were ragged but not neoplastic, and serial section likewise revealed no sign of tumor. Microscopically the ulcer was an infarct due to progressive ischemia resulting from thickening and hyalinosis of the arterial tree, many radicles of which are occluded by organizing blood clot. The vascular damage was sharply limited to the immediate vicinity of the ulcer.

A thin ring of fibrosis, much wider than the area of ulceration, extended around the colon beneath the mucosa, and produced the symmetrical marked constriction demonstrated radiographically.

Case 10:—D. K., boy, age 13. The patient complained chiefly of frequent leakage and soilage at the anal orifice, necessitating the wearing of a diaper. The abdomen was greatly distended and very hard. Anorectal examination showed a small opening about the diameter of a lead pencil immediately anterior to the anal sphincter dimple. This consisted of a fibrous tube 1.5 cm. long. A quarter-inch proctoscope encountered hard stool. The diagnosis of congenital anal atresia was made. He had submitted to a corrective operation two days after birth, again at one year and again at age six. The parents had been told that nothing further could be done.

Only a tiny catheter could be passed through the anal canal, and barium was injected through this catheter (Fig. 16). It was impossible and inadvisable to fill the entire colon with barium. The colon was so distended with fecal material and air as to completely fill the pelvis and nearly fill the entire abdomen. The diameter of the rectum was 21 cm. (8½ inches). It was evident that all of the obstruction was in the anal canal.

A long and arduous decompressive program was instituted, after which the fibrous tube was dissected upward and transplanted into the sphincter ring. An excellent result was obtained, and the boy now leads a normal existence without a diaper. Proctoscopic follow-up shows that there has been a very marked decrease in the distention of the rectum.

Discussion

Dr. A. J. Tillinghast (New York, N. Y.):—I have only a few general and rather simple comments to make, or observations to make on the presentation of this very excellent group of cases.

These cases presented really illustrate very well the problem in differential diagnosis of many constricting lesions of the colon. I think there is no question but that the utmost cooperation between the clinician, the pathologist, the radiologist, and the surgeon is necessary in all these cases in solving these problems, and, as was stated in the presentation of these cases by Dr. Van Zwalenburg, the radiologist, especially, should have all the information that can be given to him. I think in that connection, from the point of view of the radiologist, it is important to note that the radiologist must be careful to be guided by the information he gets, but not misled by it.

In the first case that was presented, the first lesion in that first case is an example. It was a case in which all the history, all the findings, pointed toward an inflammatory lesion, specifically an endometriosis, and actually the lesion was a carcinoma. This was well shown by x-ray as a typical carcinoma and correctly interpreted.

The second case was an example on the other side. The findings certainly favored a malignant lesion, that is, the physical findings, the history, and so forth, but the x-ray appearance was typical of an inflammatory lesion, and in this case it proved to be an endometriosis.

I won't cover each individual case. In general, lesions of the sigmoid are especially difficult for the radiologist to diagnose. I think, contrary to the impres-

sion I got from Dr. Van Zwalenburg's remarks, that the occurrence of carcinoma in the presence of a diverticulitis is not rare, but rather not uncommon. It certainly presents a diagnostic problem that should be attacked by the radiologist with everything at his command.

As was indicated, the radiologist should do repeated examinations. It was not indicated in the paper, that contrast air studies are important, plus spot films, and, wherever possible, spot films taken with pressure cone for visualization of mucosal structure. Those are very important and very helpful accessories.

The examination should be repeated by the radiologist and the barium enema should be repeated a number of times if the findings are not obvious at first.

The other area in the colon which was not mentioned in this paper to any extent, but where differential diagnosis is difficult, is the cecum. Here the problem is almost entirely in the hands of the radiologist. Often the laboratory findings are obscure. Often, too, cecal lesions are difficult to diagnose by the radiologist, but he does at least have some advantage in these lesions. There, the lesion is generally more accessible. He can take spot films, using pressure cone, and visualize the mucosal structure often much better than in any other location. Air studies are of value, and sometimes barium by mouth is of great value in these problems.

In general, then, I think I can summarize by saying that in addition to proctoscopy and repeated barium enemas, and eventually to exploration, as Dr. Van Zwalenburg indicated, the examination by the radiologist should be done with extreme care. It should be repeated, and should be repeated with air contrast studies, with mucosal studies, and pressure cone films of the lesion in question—and one additional thing. Very often the addition to the barium mixture of a small amount of tannic acid will give a great deal of information. It helps in evacuation of the barium, and the tannic acid will produce a much better mucosal pattern through the colon. That is important, too, when one is doing air studies. If there is a good mucosal pattern on the postevacuation film, and air studies are done following that, the examination is much more satisfactory.

Dr. Benjamin R. Van Zwalenburg (Grand Rapids, Mich.):—Dr. Tillinghast has been very kind, and I am glad that he brought up the point of making air and spot films. I should like to say that we make spot films of the rectum and rectosigmoid junction in all cases, and air films and spot films of indicated areas whenever we see anything fluoroscopically or have reason to suspect abnormality.

I should also like to stress the very frequent value of rechecking the colon after another preparation has been done. We very frequently, after having found or suspected a lesion, re-examine the next day, or after an interval of two days for repreparation.

We have not had any experience with tannic acid, preferring not to use that routinely, because it increases irritability of the colon, but we do use a suspension of barium which includes an emulsifier rather than the plain barium mixture.

Dr. Lynn A. Ferguson (Grand Rapids, Mich.):—We deeply appreciate Dr. Tillinghast's discussion and criticisms. It is very obvious that men doing gastroenterology should have full cooperation of the radiologist and the pathologist, and

vice versa. One develops that type of cooperation only with utter frankness. When we request a colon study, we try to give the radiologist, not only a brief history, but we tell him our own proctoscopic findings and record any "hunches" which we may have. In other words, he has been alerted. He, in turn, may be uncertain and request further proctoscopic studies. If biopsies are taken or specimens removed, the same type of discussion goes on between the clinician and the pathologist. The results obtained are in direct proportion to the cooperative effort of this group.

Dr. Leon T. LeWald (New York, N. Y.):—I enjoyed the discussion very much. Several of my friends have called attention to the fact, that in 1914 I was the first to make a differential diagnosis between carcinoma and diverticulitis. So in order to get the record straight I will review the facts and give the references. The case was referred to me by Dr. Robert Abbe* (incidentally the first doctor to use radium in this country). In Dr. Abbe's words, "A lawyer, aged 60 years, had a short attack of sigmoid colitis, so-called, during the past summer, followed by loss of weight, from 168 to 146 pounds. In March, 1914, a rather sudden partial obstruction occurred with acute tenderness over a hard resisting mass in the left iliac fossa". Dr. Abbe's diagnosis was carcinoma of the colon. The patient was sent to St. Luke's Hospital to be operated upon the following day. Dr. Abbe asked me to "just make an x-ray 'picture' of the carcinoma, so I can have it for my records". I did an opaque injection of the colon and reported to Dr. Abbe that I saw no evidence of carcinoma, but suspected that the man might have diverticulitis, *although the opaque enema did not show any diverticula,* and requested permission to study the case by means of an *opaque meal,* as in my experience one could not always make diverticula show by opaque enemas, as the diverticula might be filled by fecal material which would not permit the injection to run into the pockets, but that material from an opaque meal being of more firm consistency would be forced into the diverticula by the peristaltic pressure contractions of the bowel. And when the diverticula are thus filled by material from an opaque meal, as Case† states, may be determined for ten days, as in this patient. But since that time I have a record** of as long as 92 days in one case and of 52 days in another. This led to the method by some of treatment by administration of barium sulfate in small daily doses, in the belief that it would be better to have the diverticula, at least partly, filled with such an inert substance rather than ordinary bowel contents. However, I know of one case in which after the patient had been so treated for many weeks, he suddenly perforated a diverticulum and was fortunately saved by immediate surgical intervention, as he happened to be Superintendent of the hospital and thus received prompt treatment. In Dr. Abbe's case as the diverticula remained filled for ten days, and Dr. Abbe was now convinced of the diagnosis of diverticulitis, he decided to resect the involved portion of the sigmoid. This he did on April 4, 1914 follow-

*Abbe, Robert, Med. Record (N. Y.), August 1, 1914, pp. 190-191.
†Case, J. R., Bulletin, Battle Creek Sanitarium, July, 1924.
**LeWald, L. T., Radiology, January, 1925.

ing the method of Mikulicz, so that a section of bowel about five inches in length was obtained a few days later. Gross and microscopical examination by Dr. Francis Carter Wood confirmed the diagnosis of diverticulitis, and excluded all possibility of malignancy. Dr. Abbe (an artist of no mean ability) made a beautiful illustration of the specimen which is reproduced in the *Medical Record* and shows particularly well the diverticula with long necks, so well described by Dr. Kirby A. Martin*, who mentions this case in his review of the history of diverticula, in which he gives credit to the anatomist Sommering for his description in 1794 as the first one to make such an observation, followed by Cruveilhier in 1849, and then by the pathologist Virchow in 1853, and our case, from the roentgenological standpoint in 1914. Carmen† of the Mayo Clinic, Case of Battle Creek and George of Boston followed in the x-ray diagnosis. It is interesting to note that at that time some of the best surgeons in the country held that diverticulitis or diverticulosis (this latter term originated in the mind of Dr. William Luckett, a Surgeon in New York) *led to carcinoma of the colon,* and in spite of our arguments** to the contrary it took many years to dispel this erroneous conception and accept the view that *if* diverticula of the colon *are* present in a true carcinoma it is believed to be a *coincidence,* although at times there might be an exception to even *this* point of view. Only time will tell!

*M. Clin. North America, May, 1945, New York Number.

†Carmen, R. D., The Roentgen Diagnosis of Diseases of the Alimentary Canal. 2nd Edition, p. 547.

**LeWald, L. T., Right-sided Diverticulitis and Diverticulosis. Radiology, January, 1925.

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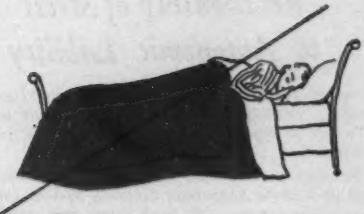

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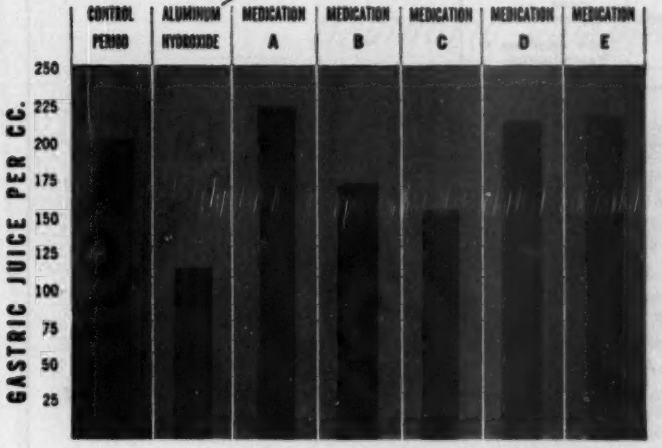

Average volume of gastric secretion from midnight to 5:30 A.M. in patients with duodenal ulcer treated with various medications *during the day only*. Aluminum hydroxide depresses volume of gastric secretion more effectively throughout entire night period. (Adapted from Brehaus, H. C., Akre, O. H., and Eyerly, J. B.: *Gastroenterology*, 16:172, Sept., 1950.)

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Relationship of Stress to Autonomic Lability

Studies in psychosomatics have shown that functional disorders often are a result of the patient's inability to adjust to emotionally stressful situations (stressor factors).

Nervous tension and chronic anxiety, discharged through a labile Autonomic Nervous System, can cause somatic disturbance. [1,2] Such states may involve any one of the organ systems or several at one time. [1,3] The outline below relates gastrointestinal and cardiovascular symptomatology to the exaggerated response of the autonomic nervous system.

	Physiologic Effects of Autonomic Discharge	
	Sympathetic	**Parasympathetic**
Gastro-intestinal	Hypomotility Intestinal Atony Hyposecretion Reduced salivation	Hypermotility Gastrointestinal spasm Hypersecretion
Cardio-vascular	Rapid heart rate Peripheral vaso-constriction	Slow heart rate Vasodilatation
Functional Manifesta-tions	Palpitation Tachycardia Elevated B. P. Dry mouth—throat	Heartburn Nausea-vomiting Low B. P. Colonic spasm

Data here tabulated is from references 3, 4, 5, 6, 7, given below.

Diagnosis of functional disorder is supported by the following indications of autonomic lability:

Variable Blood Pressure
Body Temperature Variations
Changing pulse rate
Deviations in B. M. R.
Exaggerated Cold Pressure Reflex
Glucose Tolerance Alterations

Therapy in these cases is directed toward: 1) relief of symptoms by drug therapy (so making the patient more amenable to psychotherapy); 2) psychotherapeutic guidance in making adjustment to stressful situations and correction of unhealthy attitudes.

Clinicians who have studied these disorders, including those of the menopause, report that good therapeutic results are produced by combined adrenergic (ergotamine) and cholerinergic blockade (Bellafoline) with central sedation (phenobarbital) [8,9,10]. A convenient preparation of this nature is available in the form of **Bellergal Tablets.** Functional disorders are long-term therapeutic problems; therefore, drug treatment by the following method is recommended: 5 or 6 tabs. per day for the 1st week; then gradually reduce to the smallest dose effective in maintaining the patient symptom free (average: 3 tabs. daily). Interrupt for 1 week out of every month to assess results.

1. Ebaugh, F.: Postgrad. Med. *4:* 208, 1948. 2. Wilbur, D.: J.A.M.A. *141:* 1199, 1949. 3. Williams, E. and Carmichael, C.: J. Nat'l. Med. Assoc. *42:* 32, 1950. 4. Goodman, L. and Gilman, A.: The Pharmacological Basis of Therapeutics, The Macmillan Co., 1941. 5. Katz, L. et al: Ann. Int. Med. *27:* 241, 1947. 6. Weiss, E. et al: Am. J. Psychiat. *107:* 264, 1950. 7. Alvarez, W.: Chicago Med. Soc. Bulletin, 581, 1950. 8. Rakoff, A.: A Course in Practical Therapeutics, Williams and Wilkins, 1948. 9. Karnosh, L. and Zucker, E.: A Handbook of Psychiatry, C. V. Mosby Co., 1945. 10. Harris, L.: Canad. M.A.J. *58:* 251, 1948.

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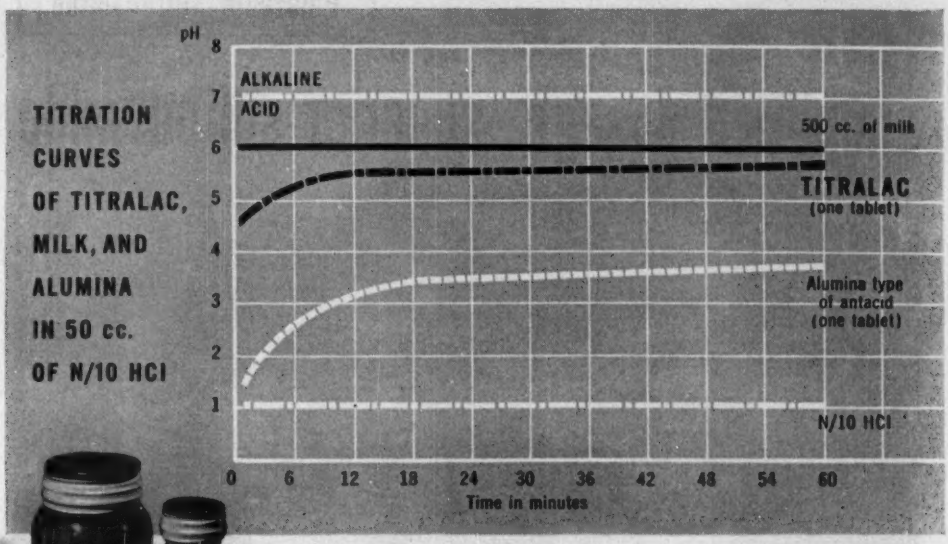

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REFERENCES

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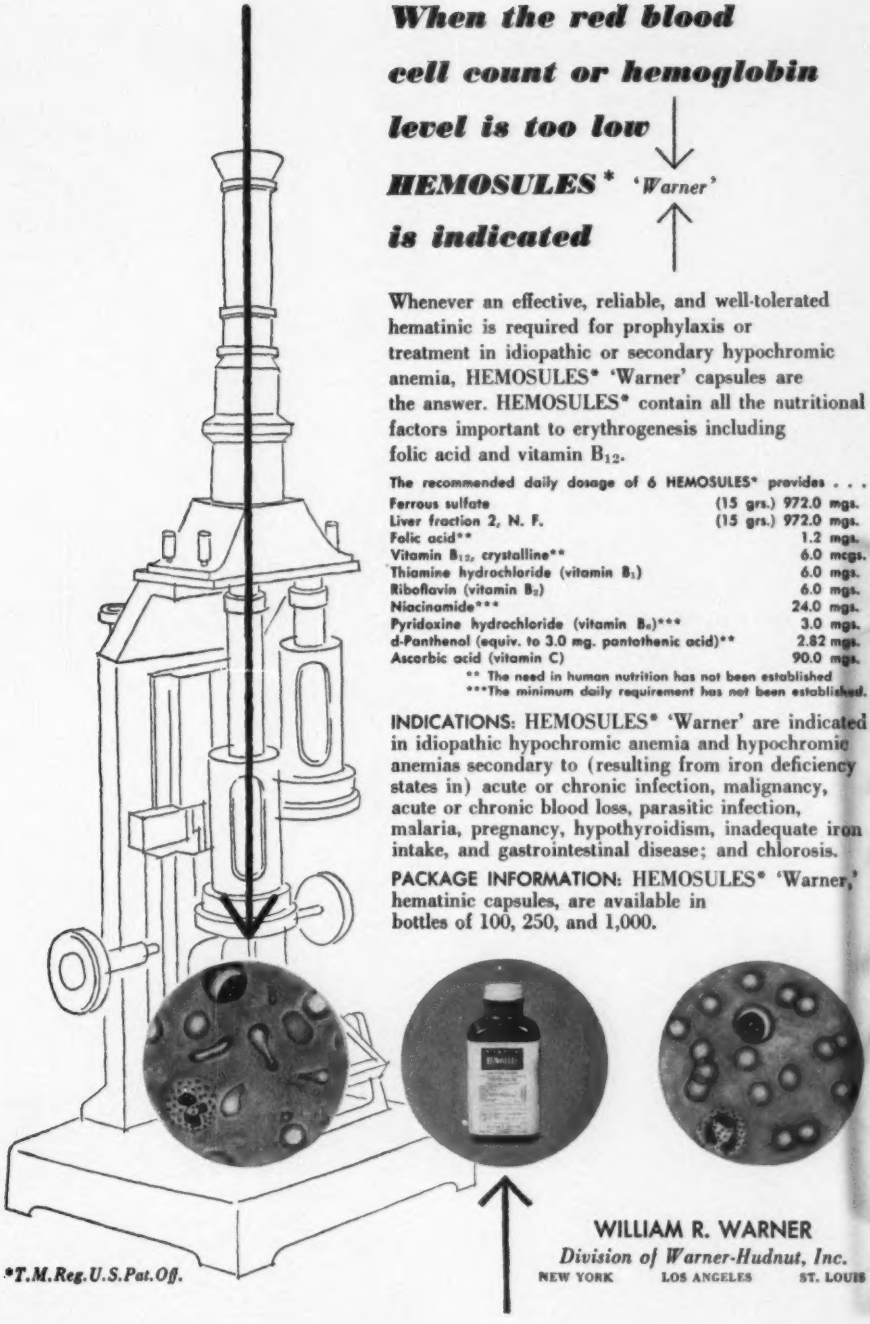

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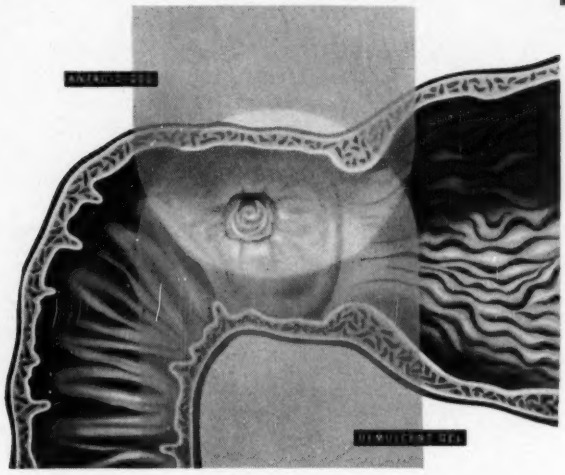

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